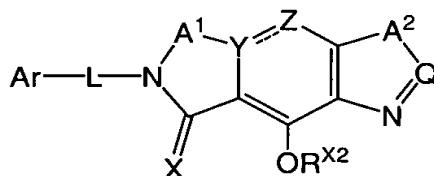


We claim:

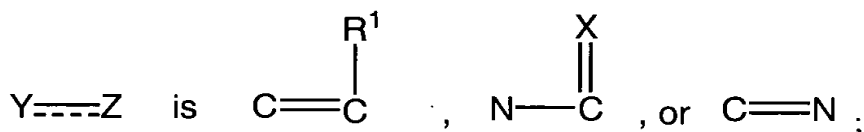
1. A compound having the structure:



wherein:

$A^1$  and  $A^2$  are independently selected from O, S, NR,  $C(R^2)_2$ ,  $CR^2OR$ ,  $CR^2OC(=O)R$ ,  $C(=O)$ ,  $C(=S)$ ,  $CR^2SR$ ,  $C(=NR)$ ,  $C(R^2)_2-C(R^3)_2$ ,  $C(R^2)=C(R^3)$ ,  $C(R^2)_2-O$ ,  $NR-C(R^3)_2$ ,  $N=C(R^3)$ ,  $N=N$ ,  $SO_2-NR$ ,  $C(=O)C(R^3)_2$ ,  $C(=O)NR$ ,  $C(R^2)_2-C(R^3)_2-C(R^3)_2$ ,  $C(R^2)=C(R^3)-C(R^3)_2$ ,  $C(R^2)C(=O)NR$ ,  $C(R^2)C(=S)NR$ ,  $C(R^2)=N-C(R^3)_2$ ,  $C(R^2)=N-NR$ , and  $N=C(R^3)-NR$ ;

Q is N,  $^+NR$ , or  $CR^4$ ;



L is selected from a bond, O, S, S-S,  $S(=O)$ ,  $S(=O)_2$ ,  $S(=O)_2NR$ , NR, N-OR,  $C_1-C_{12}$  alkylene,  $C_1-C_{12}$  substituted alkylene,  $C_2-C_{12}$  alkenylene,  $C_2-C_{12}$  substituted alkenylene,  $C_2-C_{12}$  alkynylene,  $C_2-C_{12}$  substituted alkynylene,  $C(=O)NH$ ,  $OC(=O)NH$ ,  $NHC(=O)NH$ ,  $C(=O)$ ,  $C(=O)NH(CH_2)_n$ , or  $(CH_2CH_2O)_n$ , where n may be 1, 2, 3, 4, 5, or 6;

X is selected from O, S, NH, NR, N-OR, N-NR<sub>2</sub>, N-CR<sub>2</sub>OR and N-CR<sub>2</sub>NR<sub>2</sub>;

Ar is selected from  $C_3-C_{12}$  carbocycle,  $C_3-C_{12}$  substituted carbocycle,  $C_6-C_{20}$  aryl,  $C_6-C_{20}$  substituted aryl,  $C_2-C_{20}$  heteroaryl, and  $C_2-C_{20}$  substituted heteroaryl;

$R^1$ ,  $R^2$ ,  $R^3$  and  $R^4$  are each independently selected from H, F, Cl, Br, I, OH,  $-NH_2$ ,  $-NH_3^+$ ,  $-NHR$ ,  $-NR_2$ ,  $-NR_3^+$ ,  $C_1-C_8$  alkylhalide, carboxylate, sulfate, sulfamate, sulfonate, 5-7 membered ring sultam,  $C_1-C_8$  alkylsulfonate,  $C_1-C_8$  alkylamino, 4-dialkylaminopyridinium,  $C_1-C_8$  alkylhydroxyl,  $C_1-C_8$  alkylthiol,  $-SO_2R$ ,  $-SO_2Ar$ ,  $-SOAr$ ,  $-SAr$ ,  $-SO_2NR_2$ ,  $-SOR$ ,  $-CO_2R$ ,  $-C(=O)NR_2$ , 5-7 membered ring lactam, 5-7 membered ring lactone,  $-CN$ ,  $-N_3$ ,  $-NO_2$ ,  $C_1-C_8$  alkoxy,  $C_1-C_8$  trifluoroalkyl,  $C_1-C_8$  alkyl,  $C_1-C_8$

substituted alkyl, C<sub>3</sub>–C<sub>12</sub> carbocycle, C<sub>3</sub>–C<sub>12</sub> substituted carbocycle, C<sub>6</sub>–C<sub>20</sub> aryl, C<sub>6</sub>–C<sub>20</sub> substituted aryl, C<sub>2</sub>–C<sub>20</sub> heteroaryl, and C<sub>2</sub>–C<sub>20</sub> substituted heteroaryl, polyethyleneoxy, phosphonate, phosphate, and a prodrug moiety;

when taken together on a single carbon, two R<sup>2</sup> or two R<sup>3</sup> may form a spiro ring; and

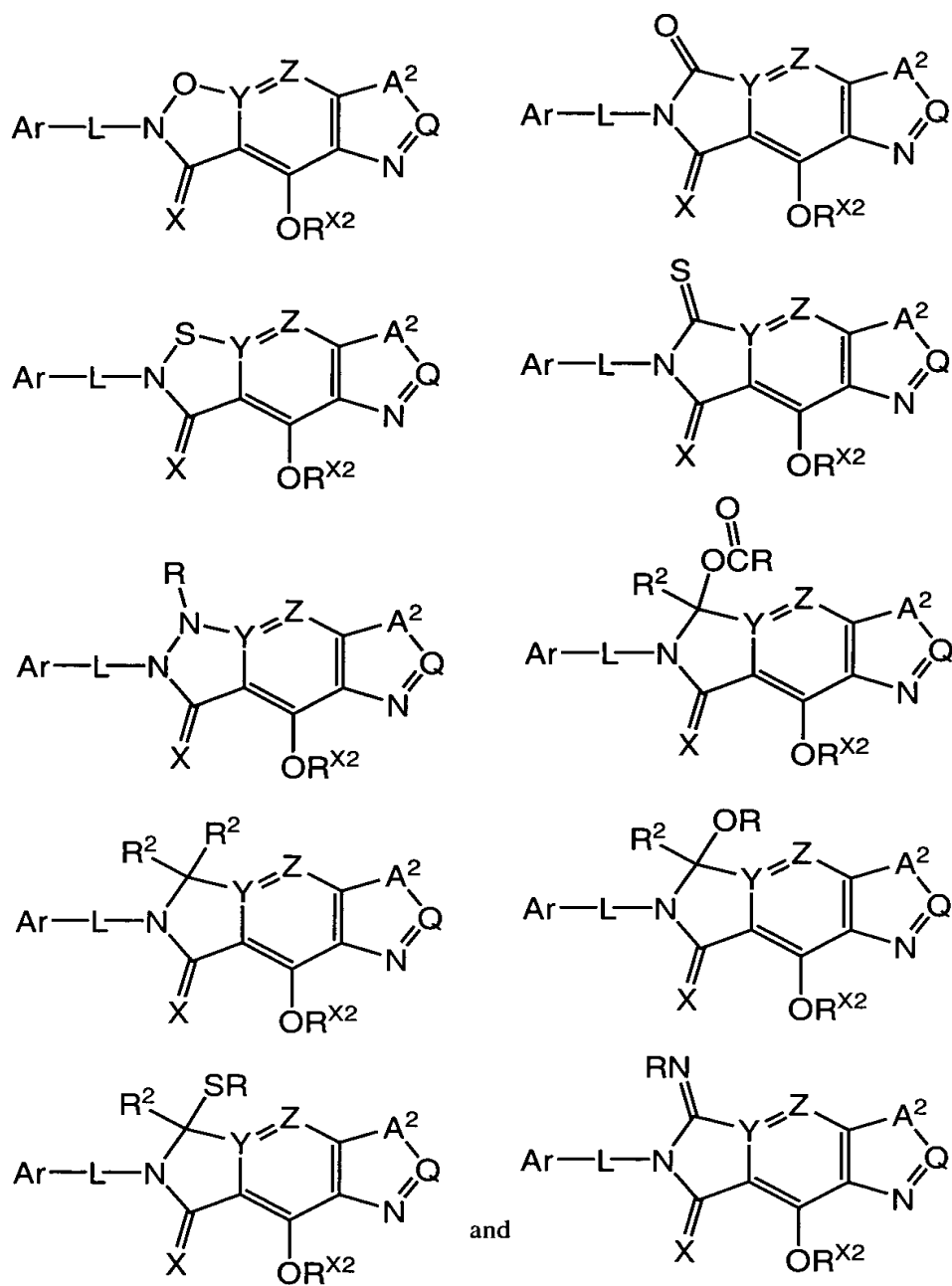
5 R is independently selected from H, C<sub>1</sub>–C<sub>8</sub> alkyl, C<sub>1</sub>–C<sub>8</sub> substituted alkyl, C<sub>6</sub>–C<sub>20</sub> aryl, C<sub>6</sub>–C<sub>20</sub> substituted aryl, C<sub>2</sub>–C<sub>20</sub> heteroaryl, and C<sub>2</sub>–C<sub>20</sub> substituted heteroaryl, polyethyleneoxy, phosphonate, phosphate, and a prodrug moiety;

R<sup>X2</sup> is independently selected from H, C<sub>1</sub>–C<sub>8</sub> alkyl, C<sub>1</sub>–C<sub>8</sub> substituted alkyl, C<sub>6</sub>–C<sub>20</sub> aryl, C<sub>6</sub>–C<sub>20</sub> substituted aryl, C<sub>2</sub>–C<sub>20</sub> heteroaryl, and C<sub>2</sub>–C<sub>20</sub> substituted heteroaryl,  
10 polyethyleneoxy, phosphonate, phosphate, a prodrug, a pharmaceutically acceptable prodrug, a prodrug moiety, a protecting group, and a phosphonate prodrug moiety;

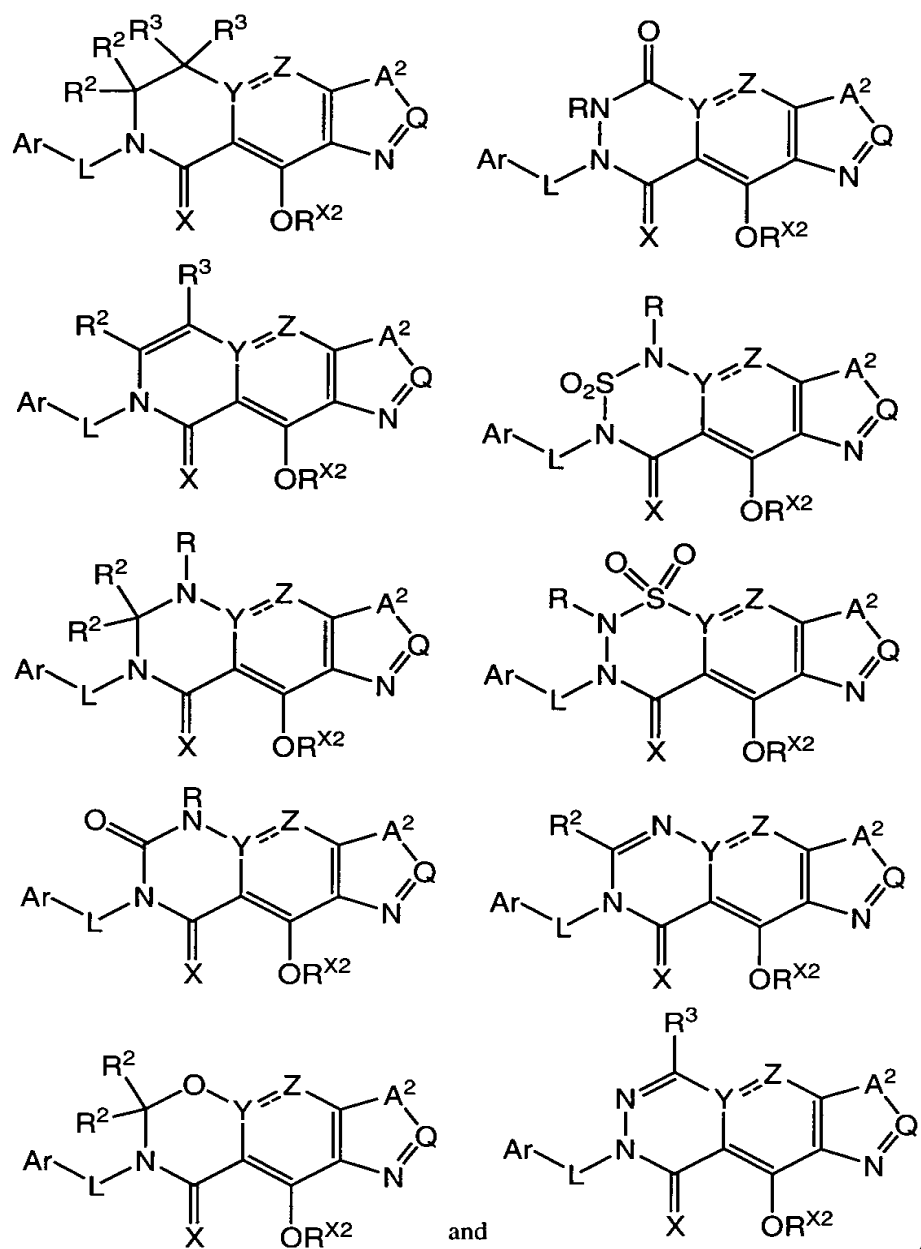
and the salts, solvates, resolved enantiomers and purified diastereomers thereof;

with the proviso that when Y=Z is C=C(OH), X is O, A<sup>1</sup> is C(=O), A<sup>2</sup> is C(R<sup>2</sup>)=C(R<sup>3</sup>), and Q is CH, then L is not a bond.

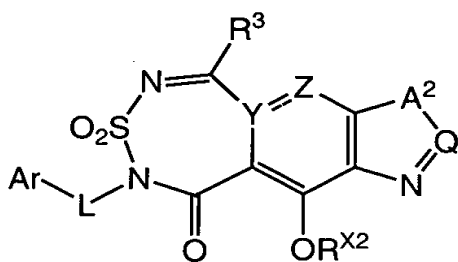
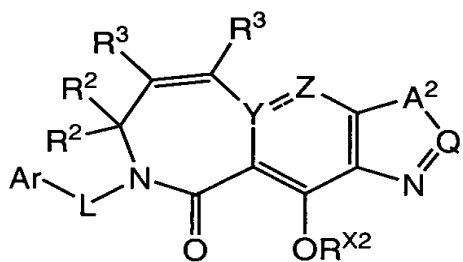
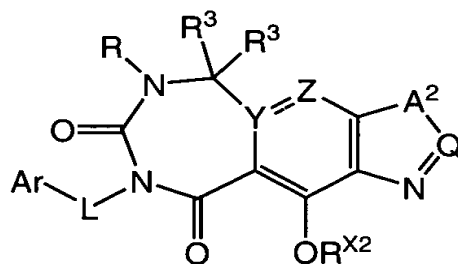
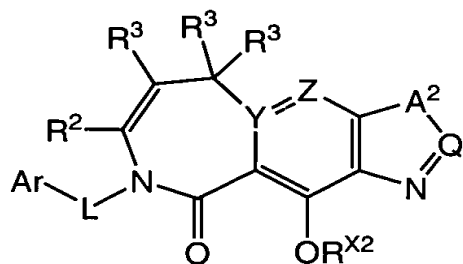
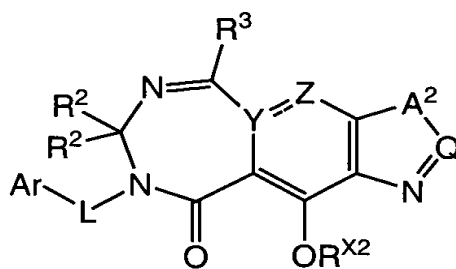
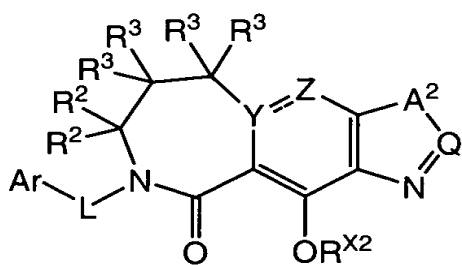
2. A compound of claim 1 selected from the structures:



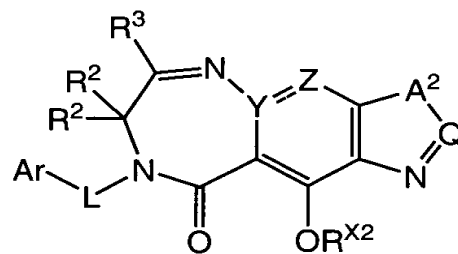
3. A compound of claim 1 selected from the structures:



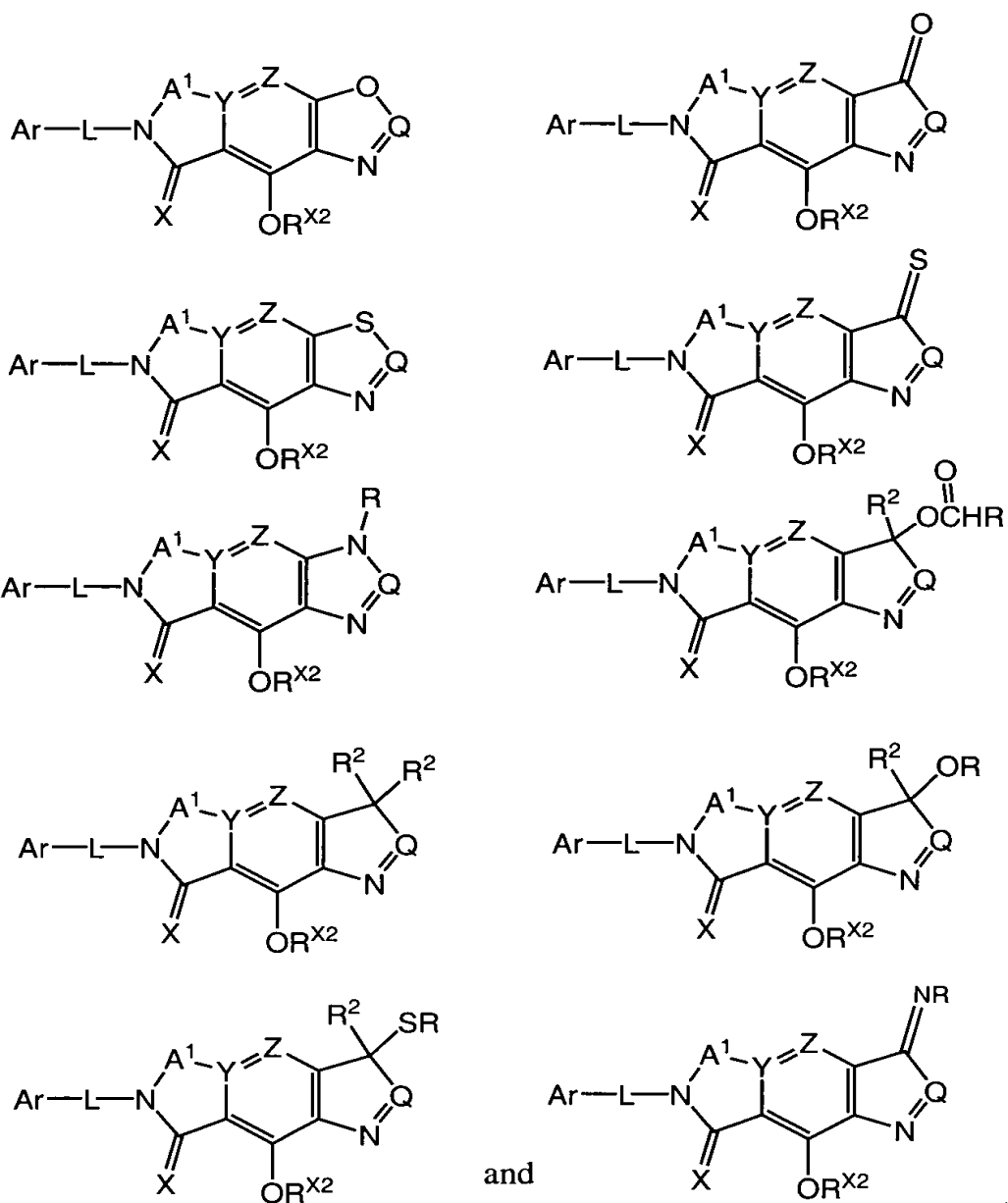
4. A compound of claim 1 selected from the structures:



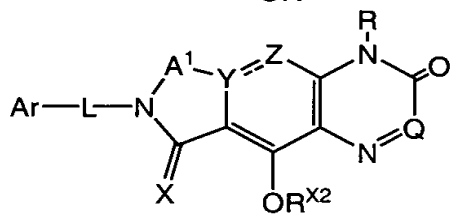
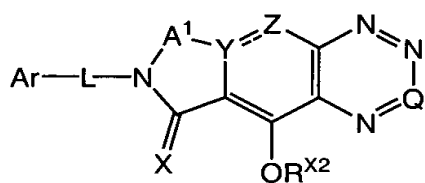
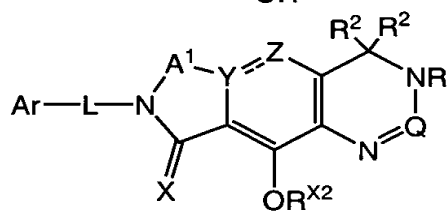
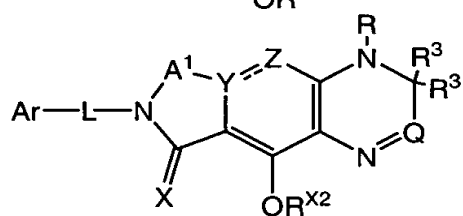
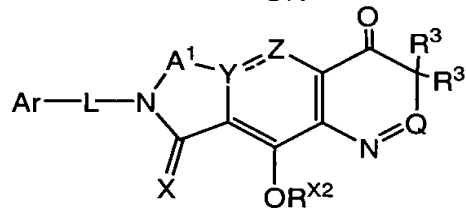
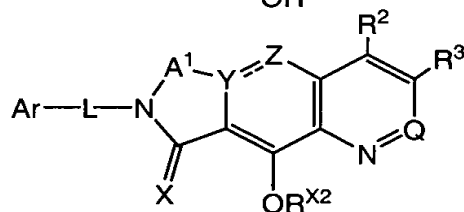
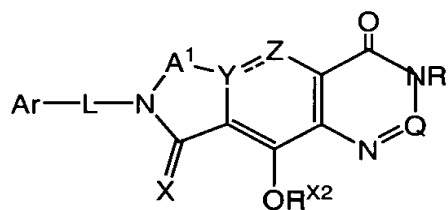
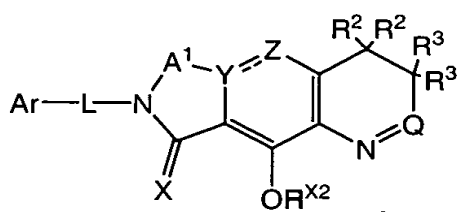
and



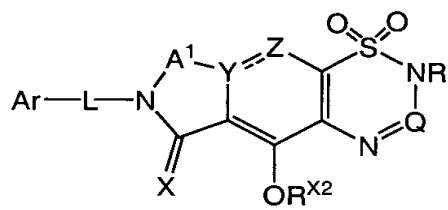
5. A compound of claim 1 selected from the structures:



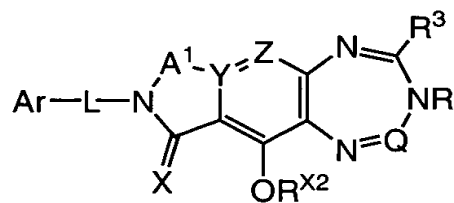
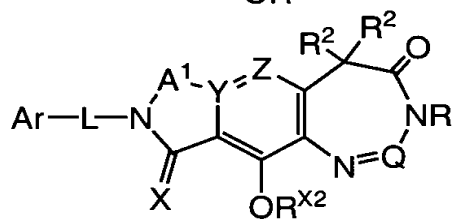
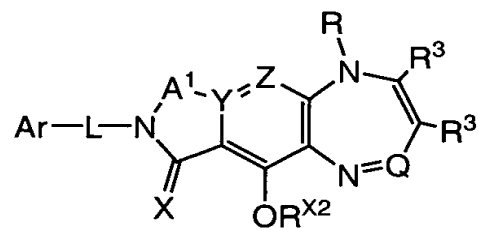
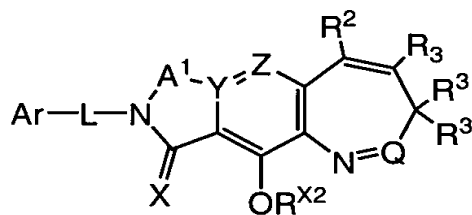
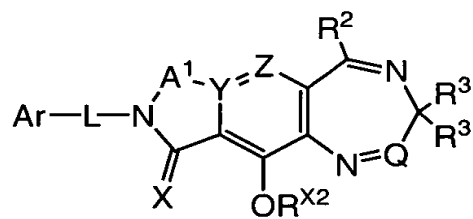
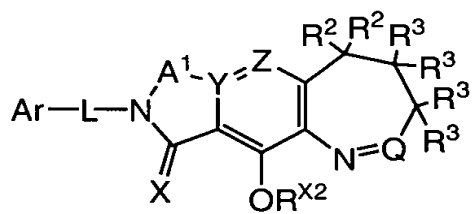
6. A compound of claim 1 selected from the structures:



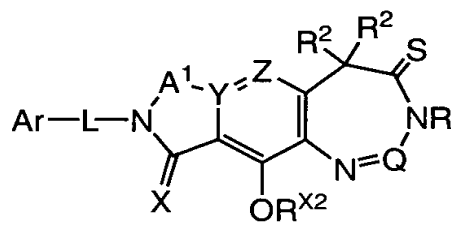
and



7. A compound of claim 1 selected from the structures:

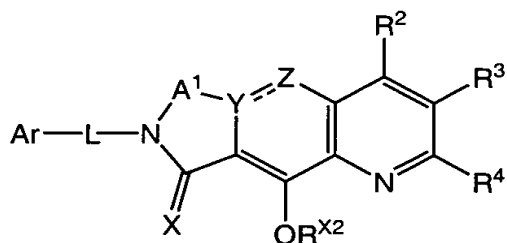


and

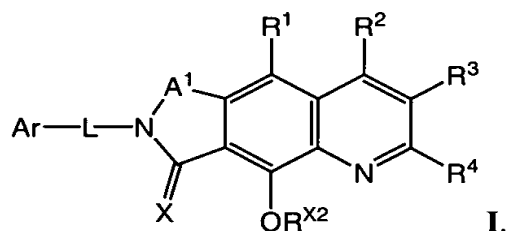




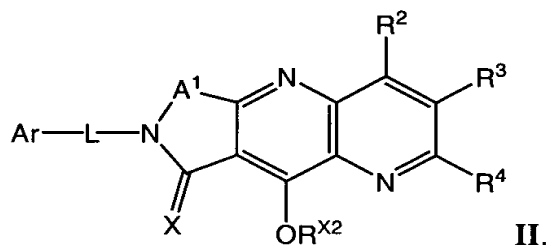
8. A compound of claim 6 having the structure:



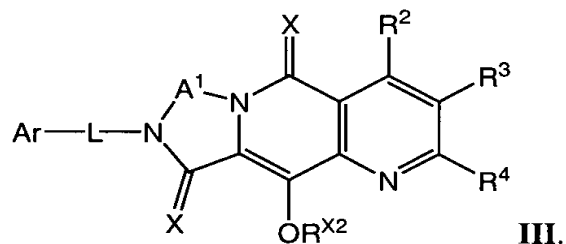
9. A compound of claim 6 having Formula I:



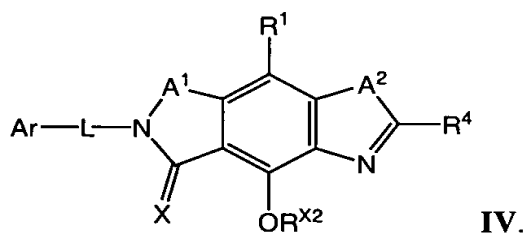
- 5 10. A compound of claim 6 having Formula II:



11. A compound of claim 6 having Formula III:

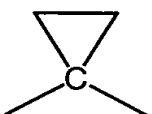


12. A compound of claim 1 having Formula IV:



13. A compound of claim 1 comprising at least one phosphonate group.

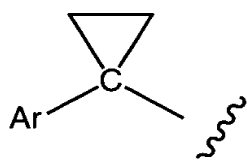
14. A compound of claim 1 wherein substituted alkyl, substituted alkylene, substituted alkylenylene, substituted alkynylene, substituted carbocycle, substituted aryl, and substituted heteroaryl are independently substituted with one or more substituents selected from F, Cl, Br, I, OH,  $-NH_2$ ,  $-NH_3^+$ ,  $-NHR$ ,  $-NR_2$ ,  $-NR_3^+$ ,  $C_1-C_8$  alkylhalide, carboxylate, sulfate, sulfamate, sulfonate, 5-7 membered ring sultam,  $C_1-C_8$  alkylsulfonate,  $C_1-C_8$  alkylamino, 4-dialkylaminopyridinium,  $C_1-C_8$  alkylhydroxyl,  $C_1-C_8$  alkylthiol,  $-SO_2R$ ,  $-SO_2Ar$ ,  $-SOAr$ ,  $-SAr$ ,  $-SO_2NR_2$ ,  $-SOR$ ,  $-CO_2R$ ,  $-C(=O)NR_2$ , 5-7 membered ring lactam, 5-7 membered ring lactone,  $-CN$ ,  $-N_3$ ,  $-NO_2$ ,  $C_1-C_8$  alkoxy,  $C_1-C_8$  trifluoroalkyl,  $C_1-C_8$  alkyl,  $C_3-C_{12}$  carbocycle,  $C_6-C_{20}$  aryl,  $C_2-C_{20}$  heteroaryl, polyethyleneoxy, phosphonate, phosphate, and a prodrug moiety.

15. The compound of claim 1 wherein  $A^1$  is  $CH_2$ ,  $C(CH_3)_2$ , ,  $CH_2-CH_2$ ,  $C(CH_3)_2-CH_2$ , or  $CH_2-CH_2-CH_2$ .

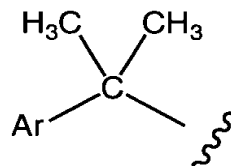
16. The compound of claim 9 wherein X is O; L is  $CH_2$ ; and Ar is substituted phenyl.

17. The compound of claim 16 wherein Ar is 4-fluorophenyl.
18. The compound of claim 9 wherein X is O; and  $R^2$ ,  $R^3$  and  $R^4$  are each H.
19. The compound of claim 9 wherein X is O;  $A^1$  is  $CH_2$ ; and  $R^2$ ,  $R^3$  and  $R^4$  are each H.

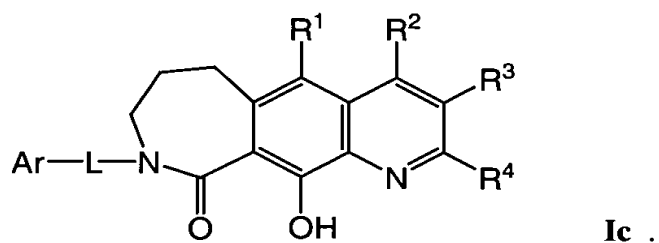
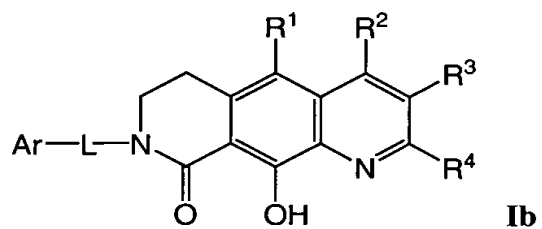
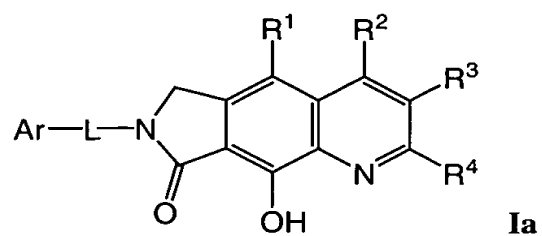
20. The compound of claim 1 wherein Ar-L is selected from the structures:



and

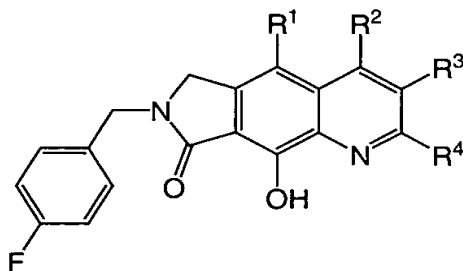


21. A compound of claim 9 comprising Formula Ia, Ib, or Ic:

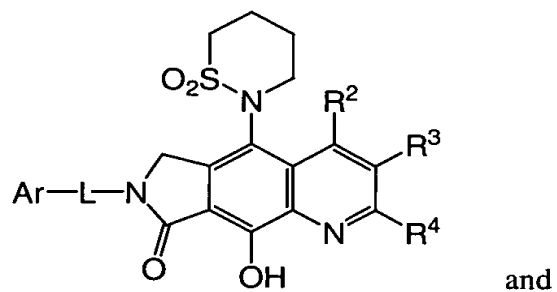


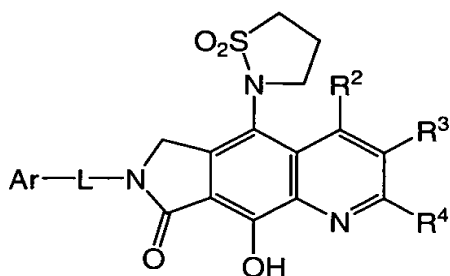
5

22. A compound of claim 9 having the structure:

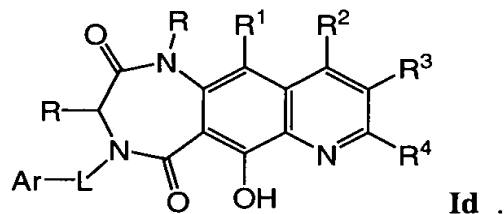


23. A compound of claim 22 selected from the structures:

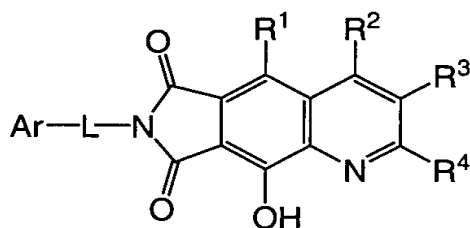




24. A compound of claim 9 having Formula Id:



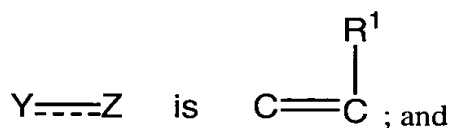
25. A compound of claim 9 having the structure:



5

with the proviso that when  $R^1$  is OH, and  $R^2$ ,  $R^3$ , and  $R^4$  are H, then L is not a bond.

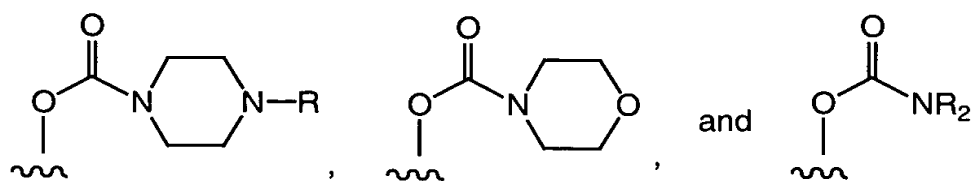
26. A compound of claim 1 wherein



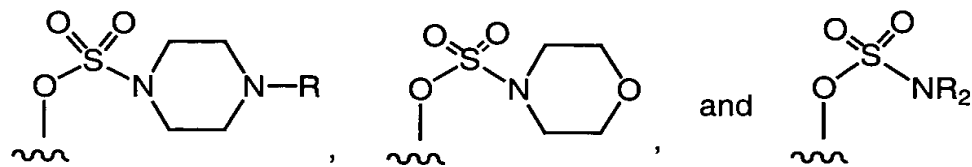
$R^1$  is  $\text{CR}_3$ ,  $\text{C}(=\text{O})\text{NR}_2$ ,  $\text{OC}(=\text{O})\text{OR}$ ,  $\text{OC}(=\text{O})\text{NR}_2$ ,  $\text{OC}(=\text{O})\text{R}$ ,  $\text{OSO}_2\text{NR}_2$  (sulfamate),  
 10  $\text{NR}_2$ ,  $\text{NRSO}_2\text{R}$ ,  $\text{SR}$ ,  $\text{S}(\text{O})\text{R}$ ,  $\text{SO}_2\text{R}$  or  $\text{SO}_2\text{NR}_2$  (sulfonamide).

27. The compound of claim 26 wherein at least one R comprises a prodrug moiety.

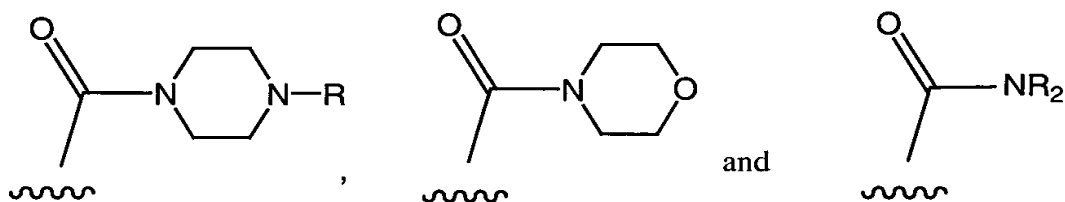
28. A compound of claim 1 wherein at least one of  $R^1$ ,  $R^2$ ,  $R^3$ , and  $R^4$  is selected from the structures:



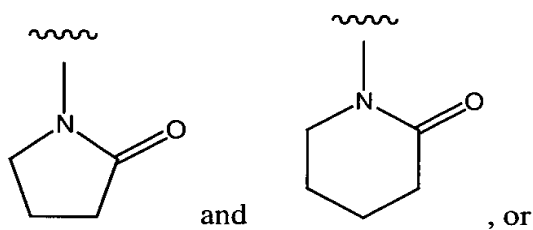
29. A compound of claim 1 wherein at least one of  $R^1$ ,  $R^2$ ,  $R^3$ , and  $R^4$  is selected from the structures:



5 30. A compound of claim 1 wherein at least one of  $R^1$ ,  $R^2$ ,  $R^3$ , and  $R^4$  is selected from the structures:

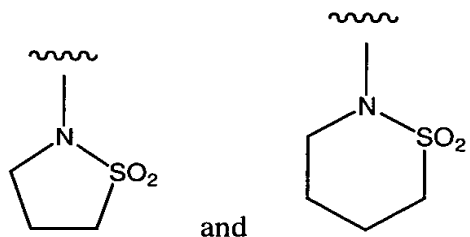


31. A compound of claim 1 wherein at least one of  $R^1$ ,  $R^2$ ,  $R^3$ , and  $R^4$  comprise a lactam having the structures:

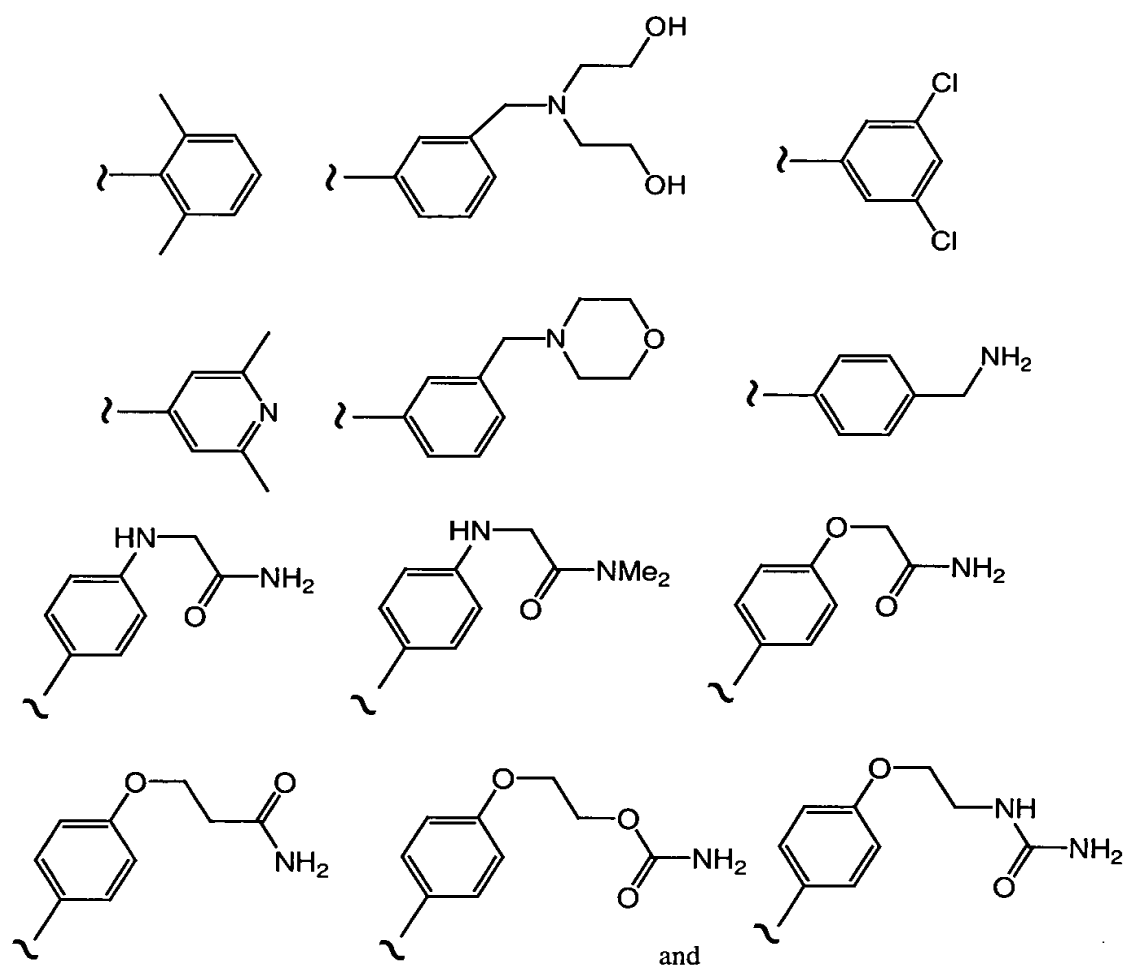


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a sultam having the structures:



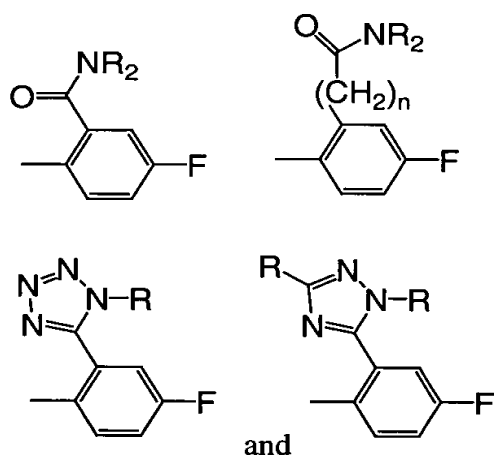
32. A compound of claim 1 wherein Ar is selected from the structures:



where the wavy line indicates the covalent attachment site to L.

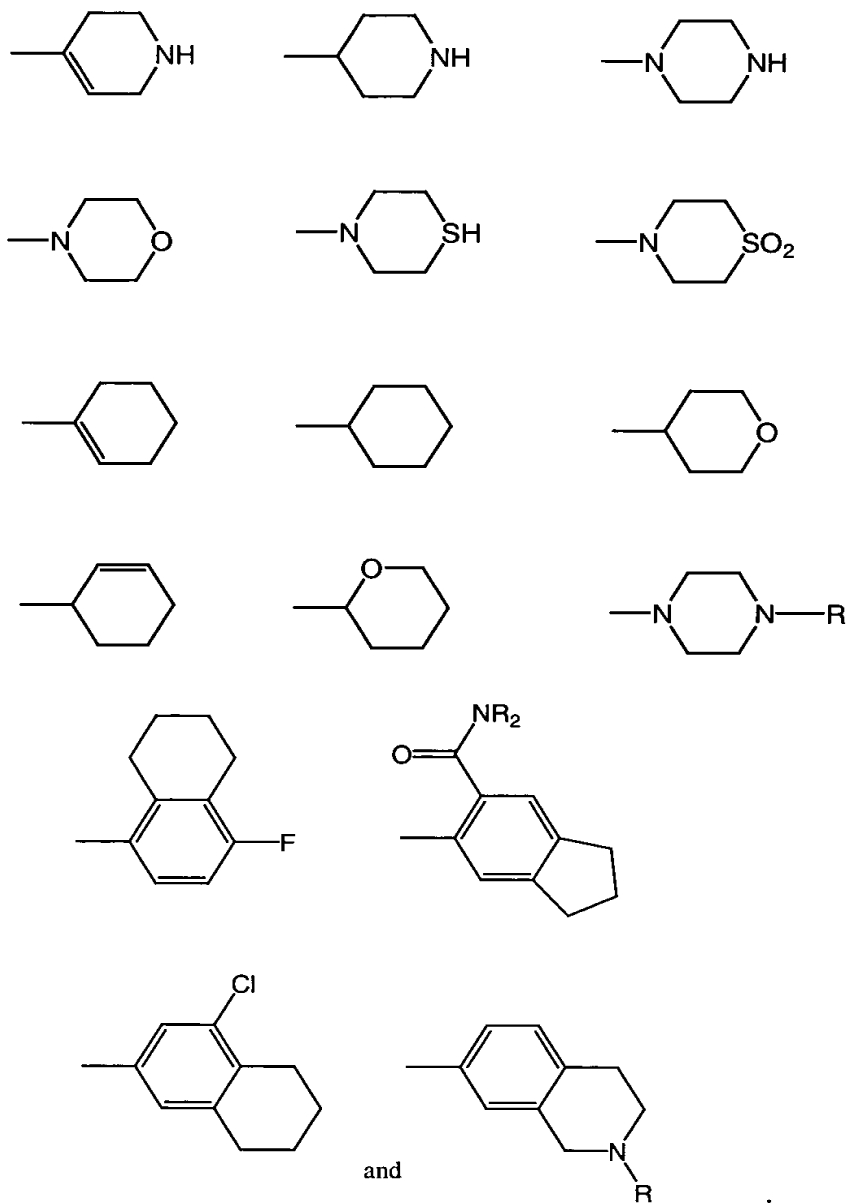
33. A compound of claim 1 wherein Ar is selected from the structures:

5

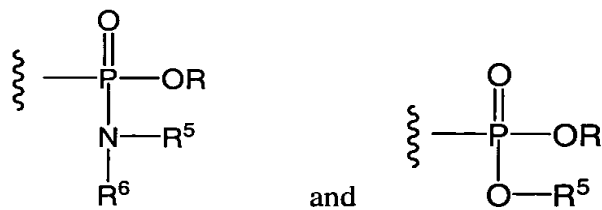


where n is 1 to 6.

34. A compound of claim 1 wherein Ar is selected from the structures:

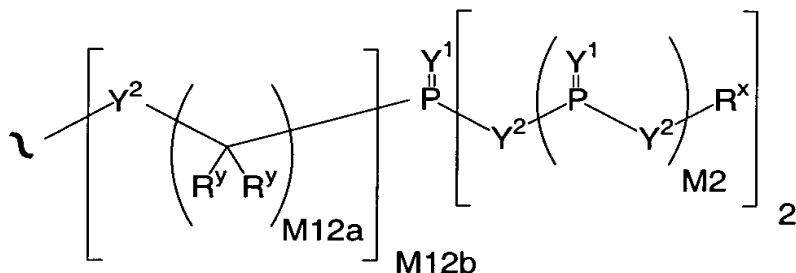


5 35. A compound of claim 1 comprising a prodrug moiety selected from the structures:



wherein  $R^5$  is  $-CR_2CO_2R^7$  where  $R^6$  and  $R^7$  are independently H or  $C_1-C_8$  alkyl.

36. The compound of claim 1 comprising a phosphonate or prodrug moiety having the structure:



wherein:

$Y^1$  is independently O, S,  $N(R^x)$ ,  $N(O)(R^x)$ ,  $N(OR^x)$ ,  $N(O)(OR^x)$ , or  $N(N(R^x)_2)$ ;

$Y^2$  is independently a bond, O,  $N(R^x)$ ,  $N(O)(R^x)$ ,  $N(OR^x)$ ,  $N(O)(OR^x)$ ,  $N(N(R^x)_2)$ , -S(O)- (sulfoxide),  $-S(O)_2-$  (sulfone), -S- (sulfide), or -S-S- (disulfide);

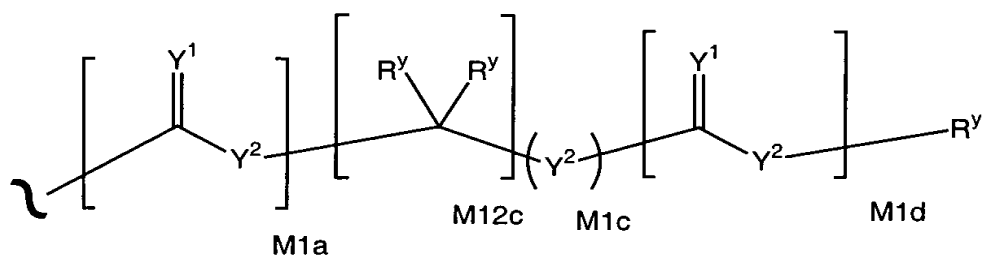
M2 is 0, 1 or 2;

M12a is 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, or 12;

M12b is 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, or 12;

$R^y$  is independently H,  $C_1-C_6$  alkyl,  $C_1-C_6$  substituted alkyl,  $C_6-C_{20}$  aryl,  $C_6-C_{20}$  substituted aryl, or a protecting group, or where taken together at a carbon atom, two vicinal  $R^y$  groups form a carbocycle or a heterocycle; and

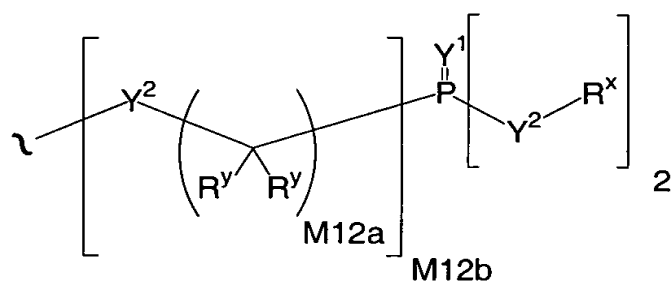
$R^x$  is independently H,  $C_1-C_6$  alkyl,  $C_1-C_6$  substituted alkyl,  $C_6-C_{20}$  aryl,  $C_6-C_{20}$  substituted aryl, or a protecting group, or the formula:



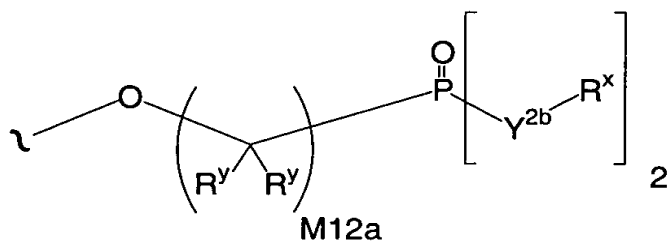
where M1a, M1c, and M1d are independently 0 or 1, and M12c is 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11 or 12.

37. The compound of claim 36 wherein the phosphonate or prodrug moiety has the structure:



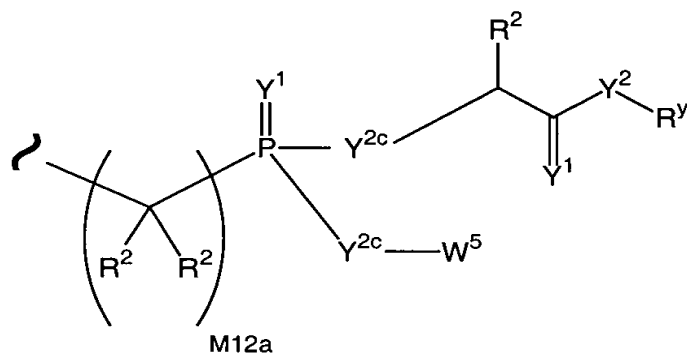


38. The compound of claim 37 wherein the phosphonate or prodrug moiety has the structure:



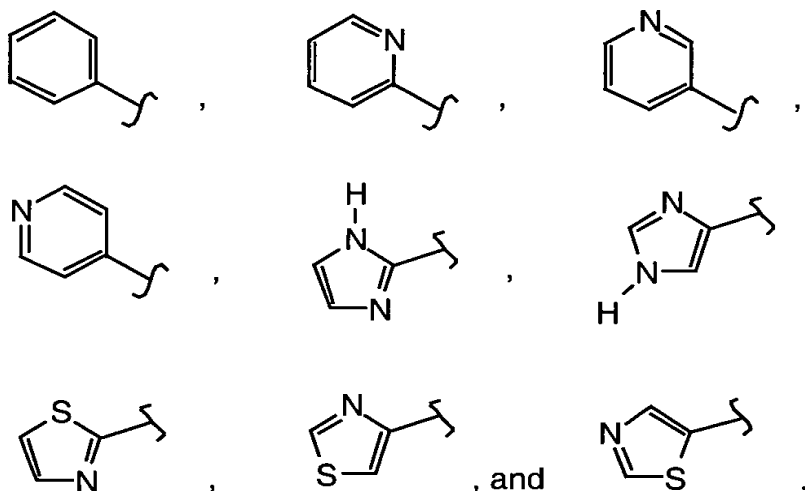
5 where  $Y^{2b}$  is O or  $N(R^x)$ .

39. The compound of claim 37 wherein the phosphonate or prodrug moiety has the structure:

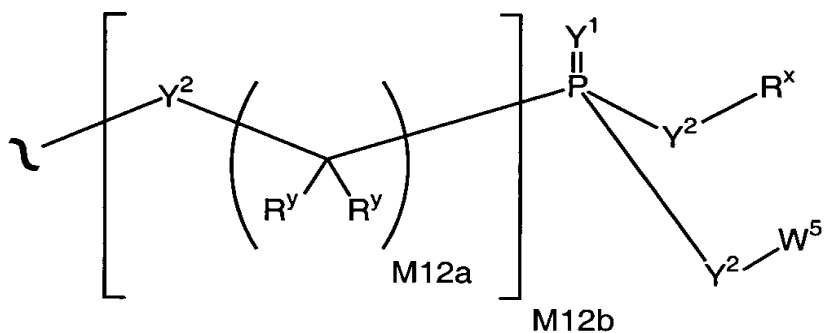


where  $W^5$  is a carbocycle, and  $Y^{2c}$  is O,  $N(R^y)$  or S.

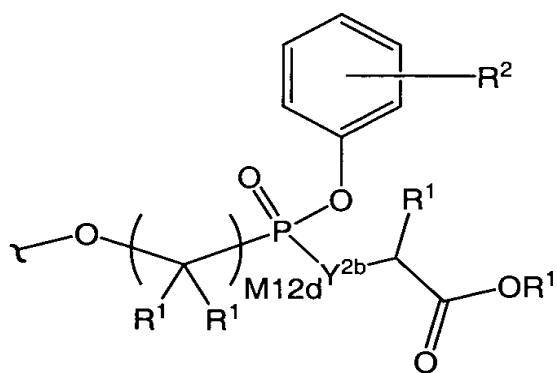
10 40. The compound of claim 39 wherein  $W^5$  is selected from the structures:



41. The compound of claim 37 wherein the phosphonate or prodrug moiety has the structure:

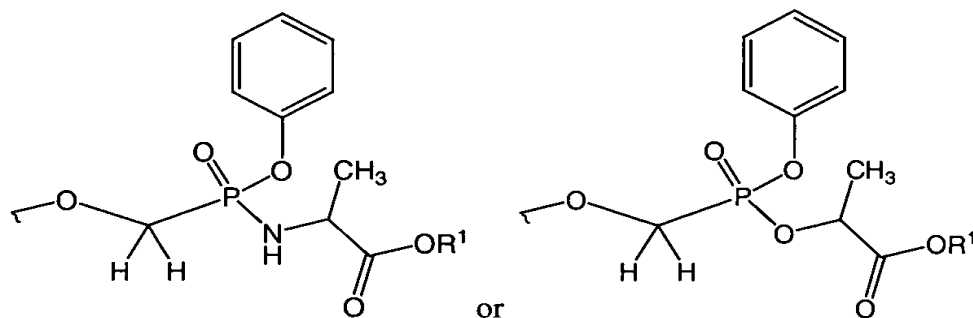


5 42. The compound of claim 41 wherein the phosphonate or prodrug moiety has the structure:

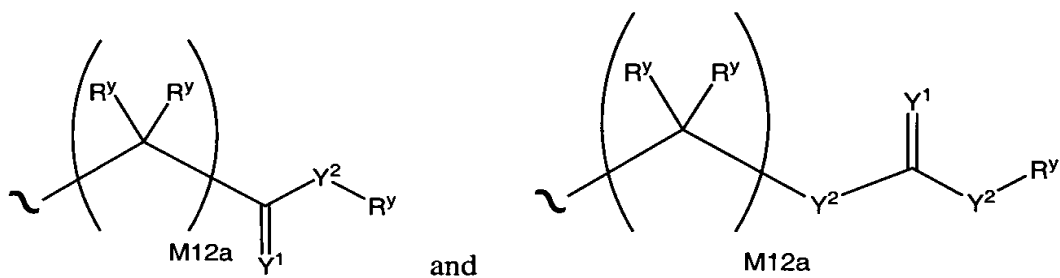


wherein  $Y^{2b}$  is O or  $N(R^x)$ ; M12d is 1, 2, 3, 4, 5, 6, 7 or 8;  $R^1$  is H or  $C_1-C_6$  alkyl; and the phenyl carbocycle is substituted with 0 to 3  $R^2$  groups where  $R^2$  is  $C_1-C_6$  alkyl or substituted alkyl.

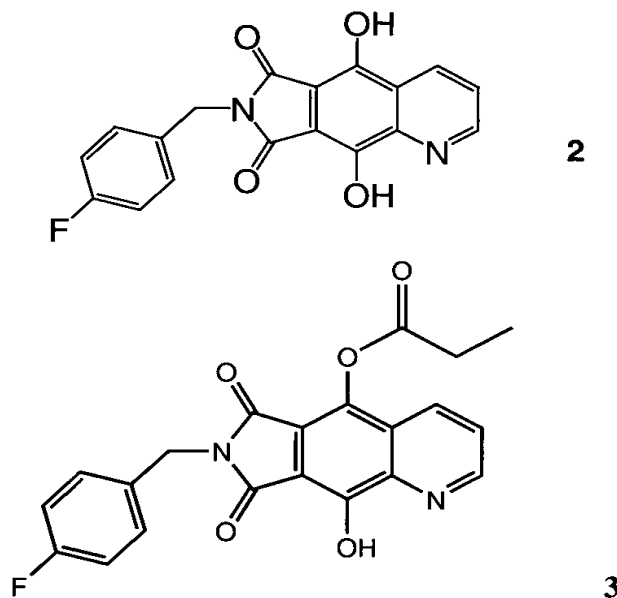
43. The compound of claim 42 wherein the phosphonate or prodrug moiety has the structure:

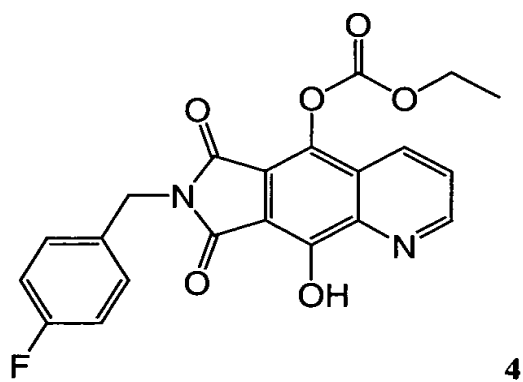


44. The compound of claim 36 wherein R<sup>x</sup> is selected from the structures:

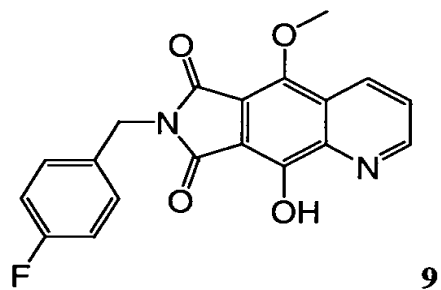


45. A compound of claim 9 selected from the structures:

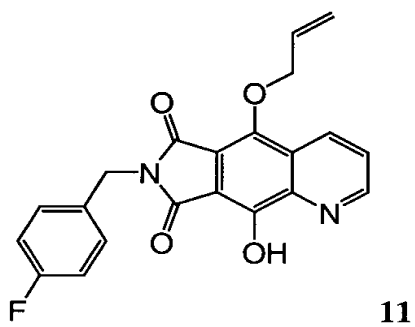




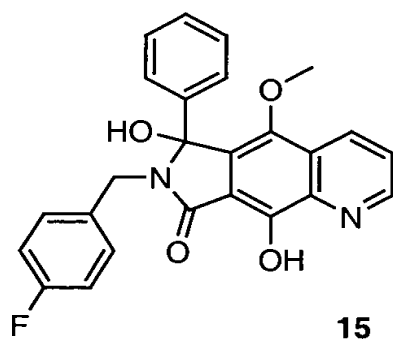
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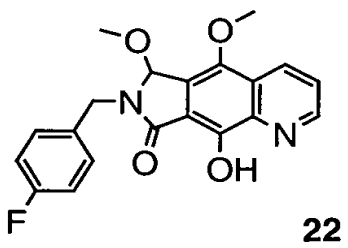
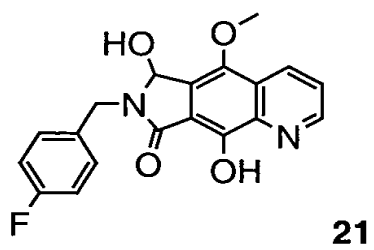
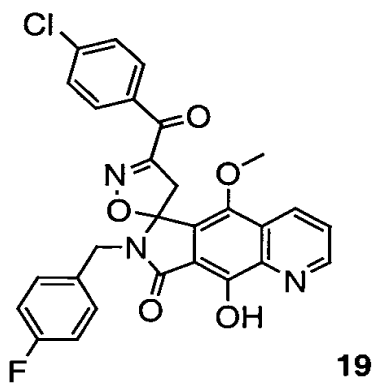
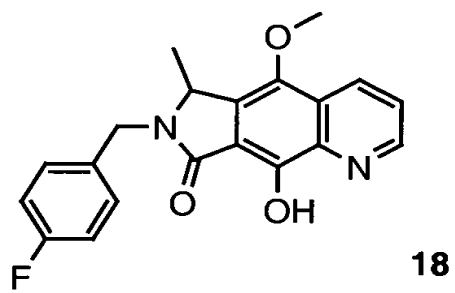
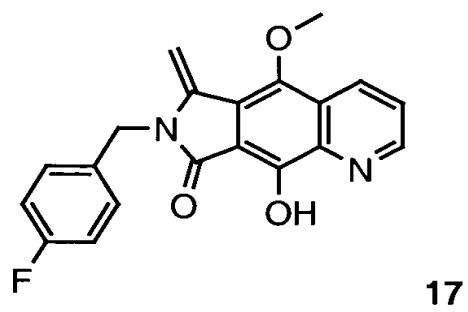
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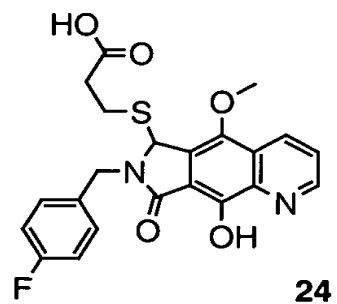
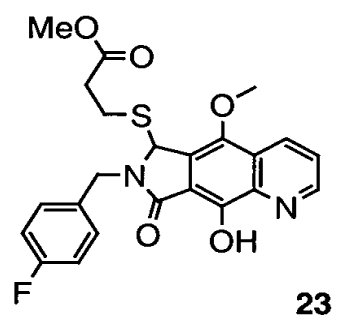


11

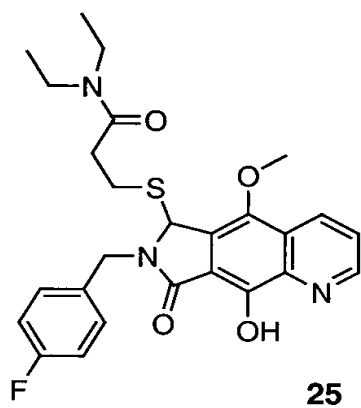


15

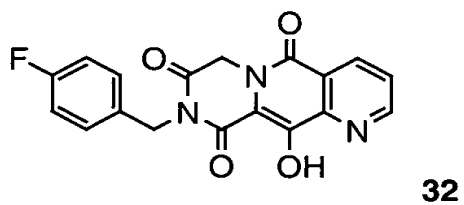




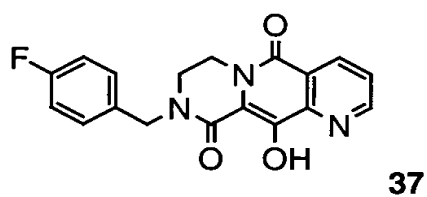
and



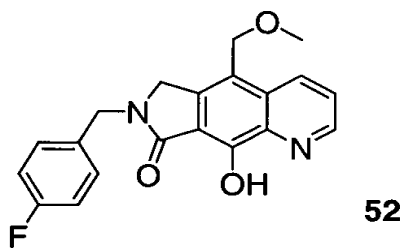
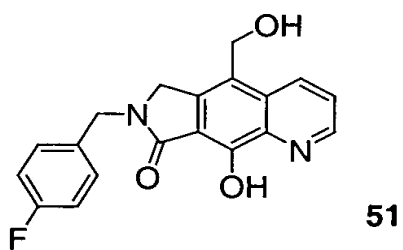
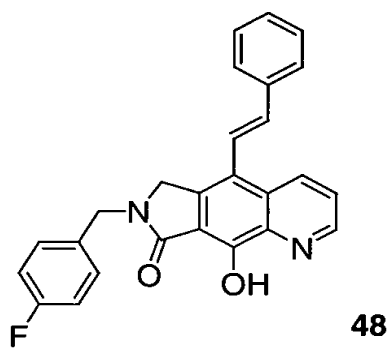
46. A compound of claim 11 selected from the structures:

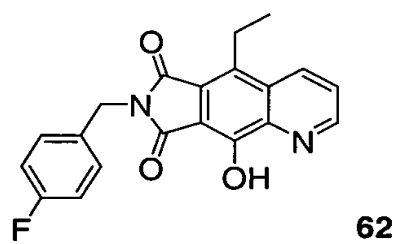
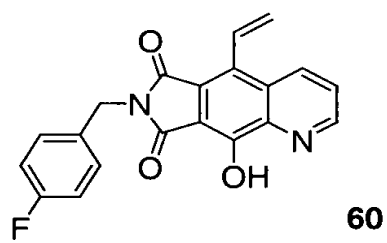
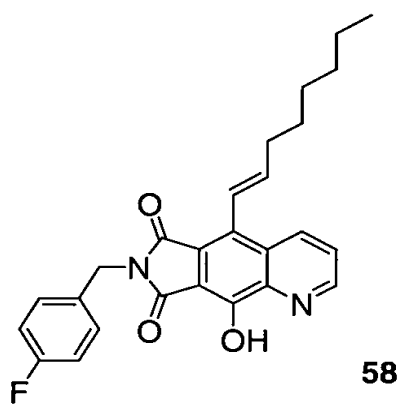
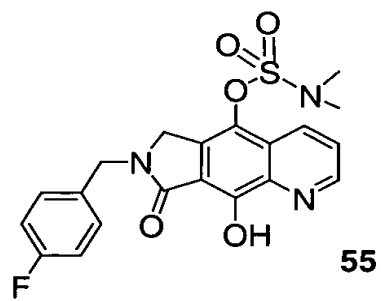
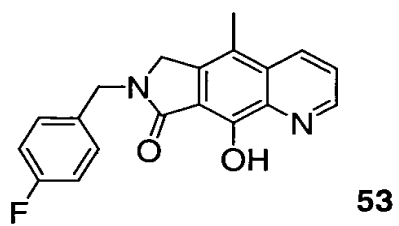


and

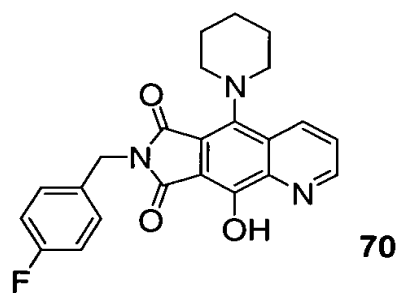
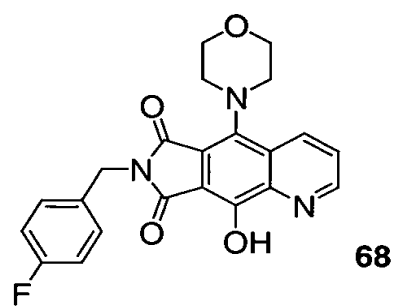
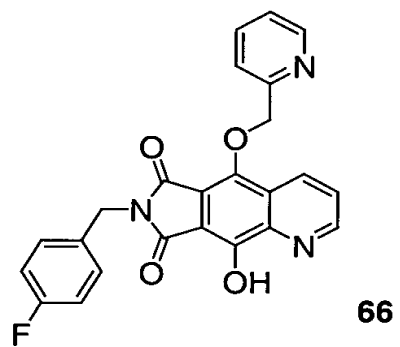
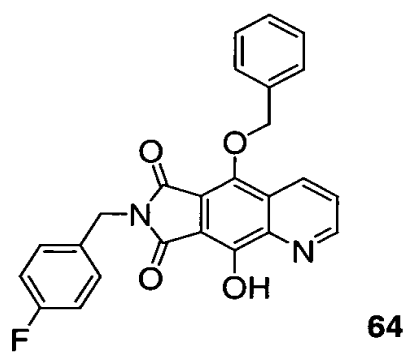


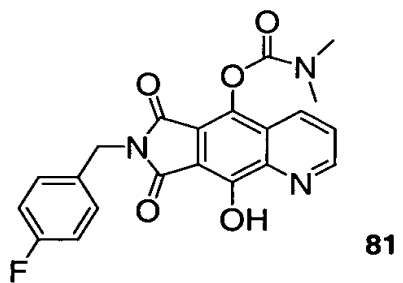
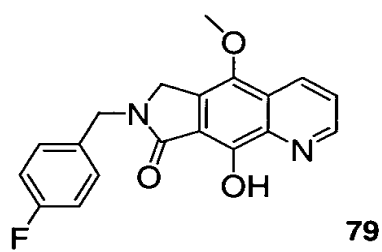
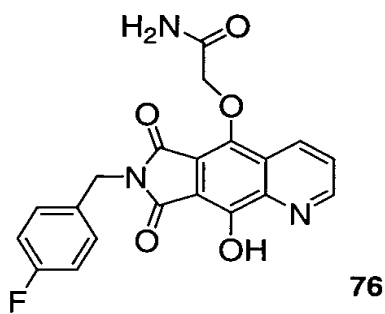
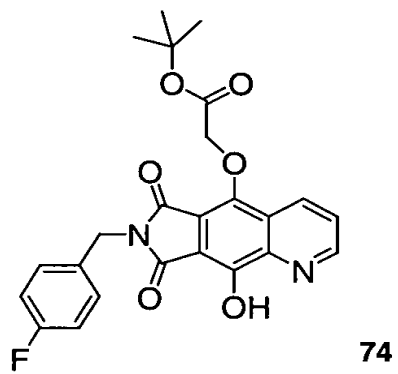
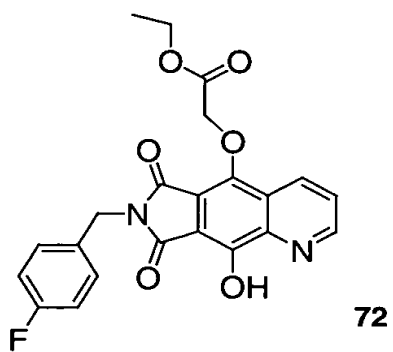
- 5 47. A compound of claim 9 selected from the structures:

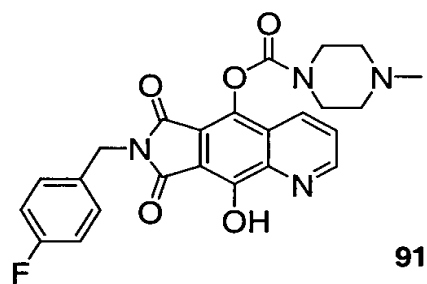
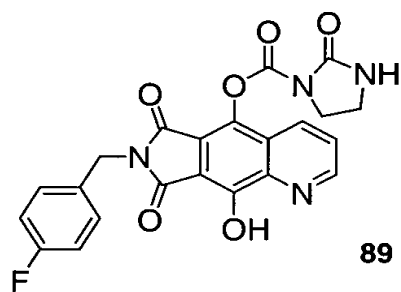
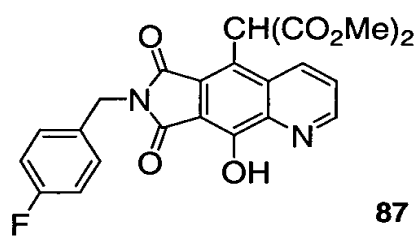
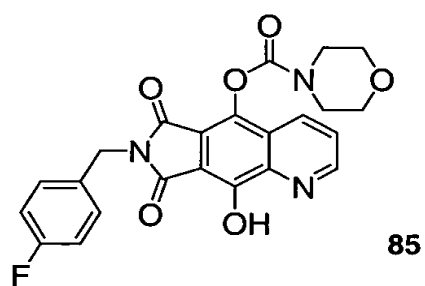
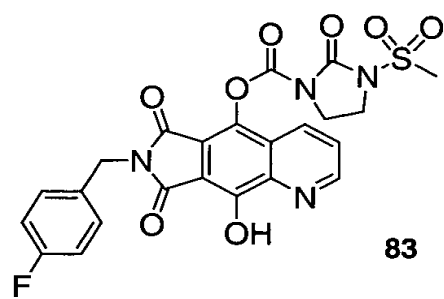


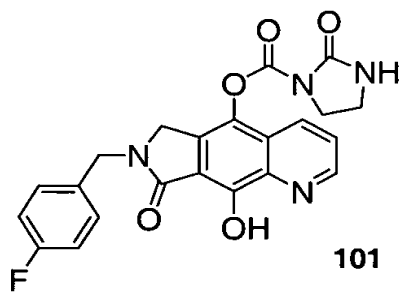
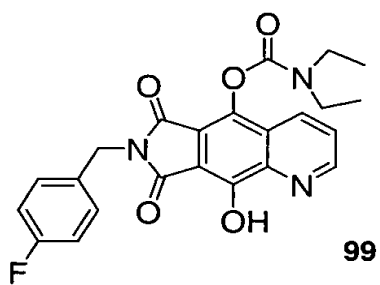
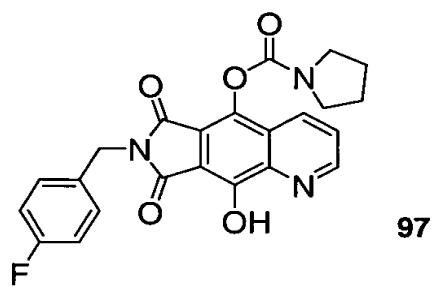
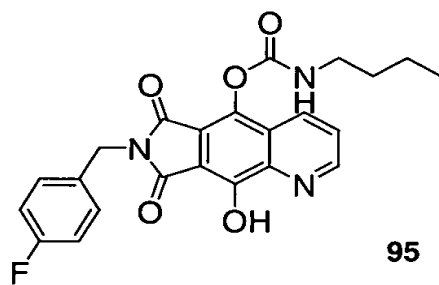
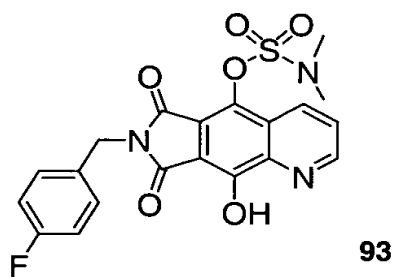


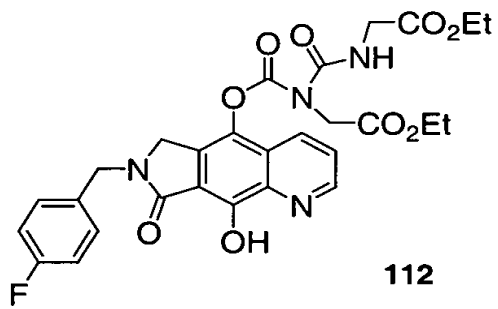
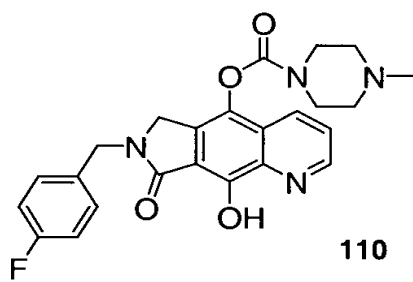
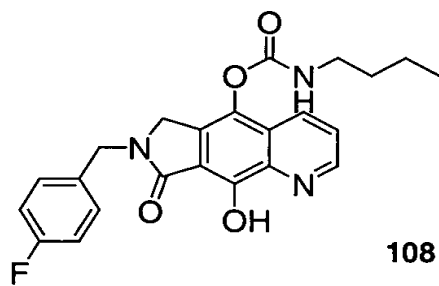
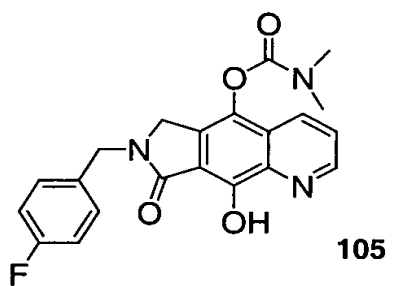
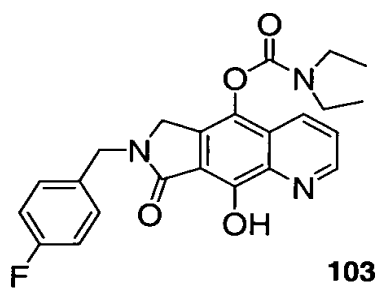


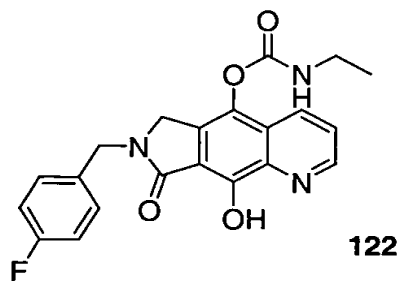
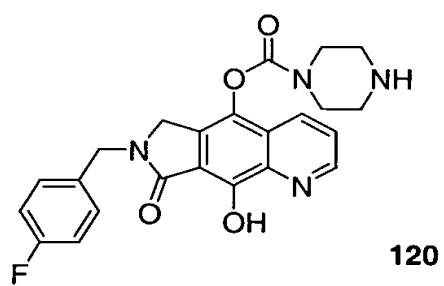
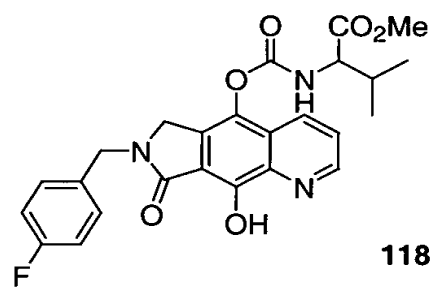
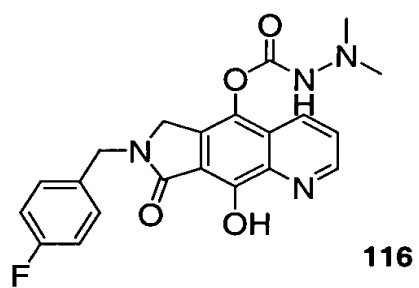
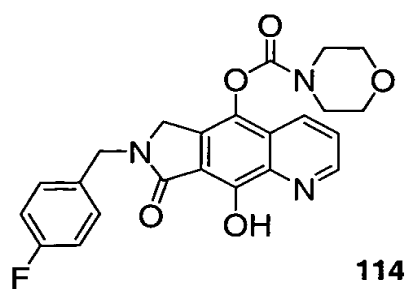


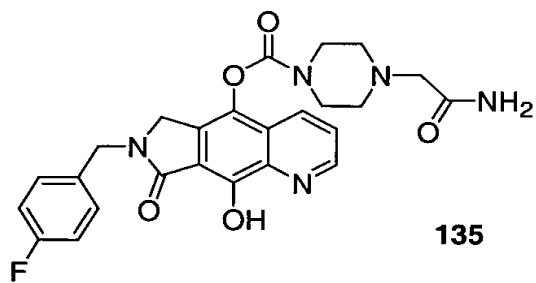
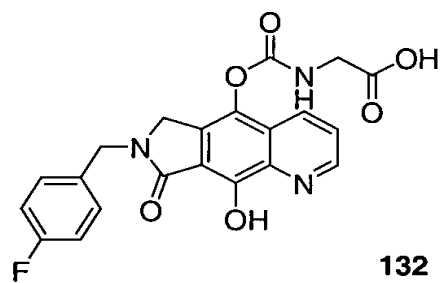
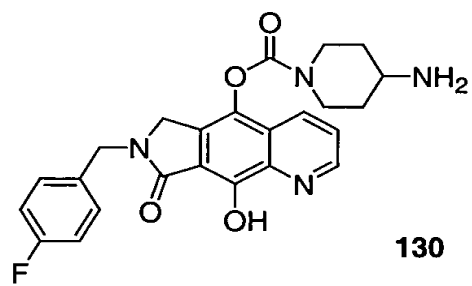
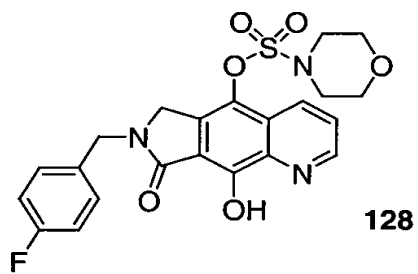
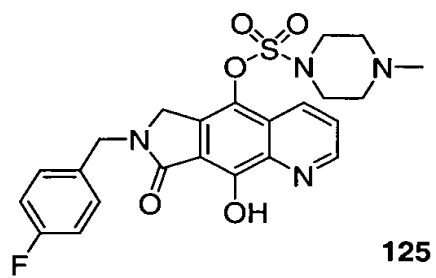


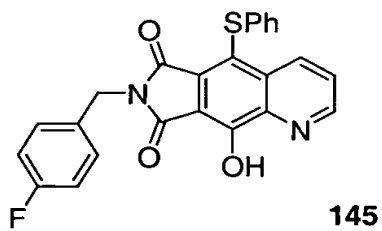
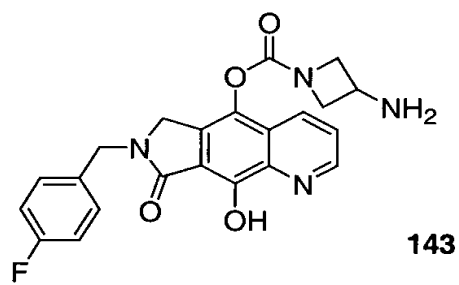
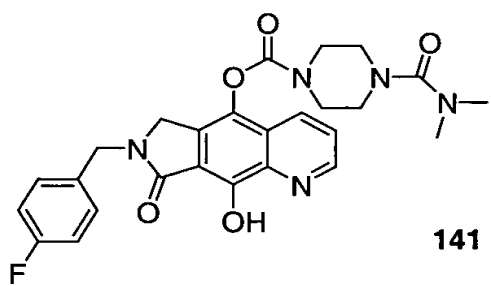
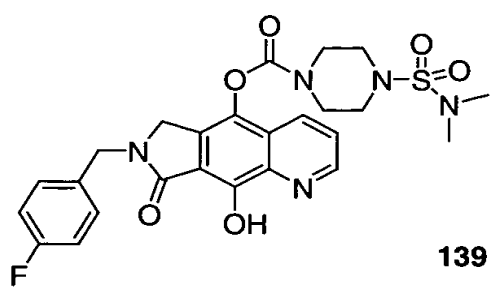
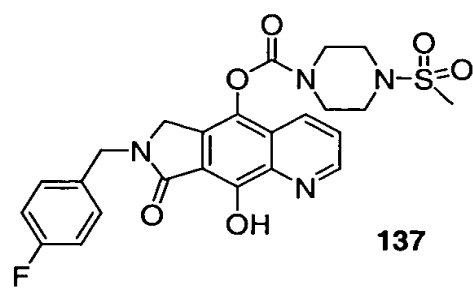




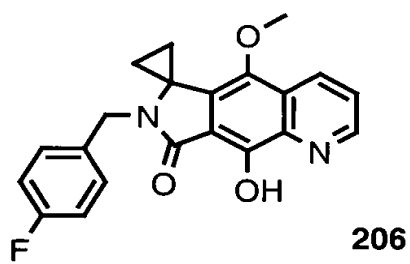
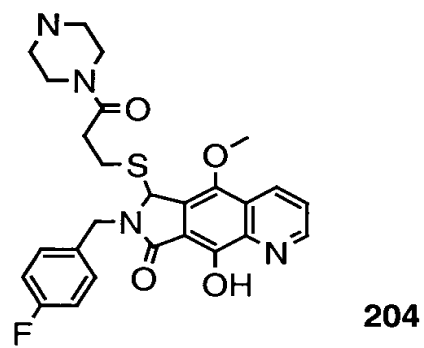
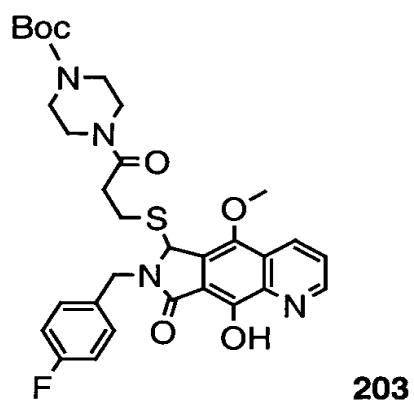
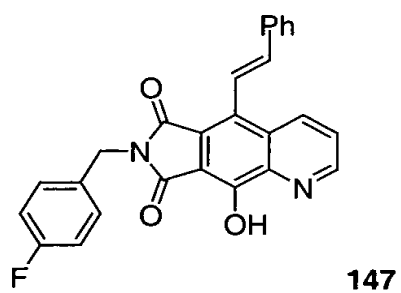


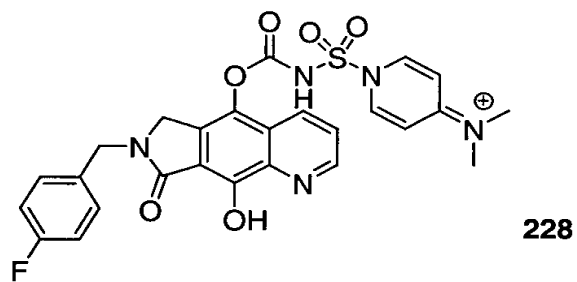
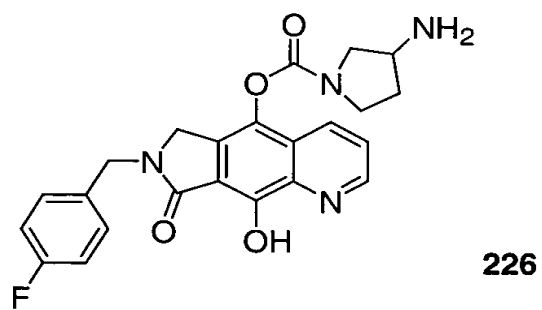
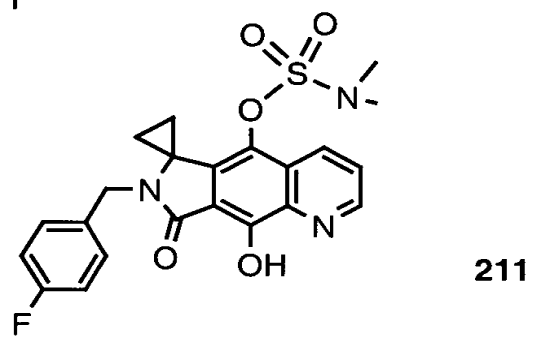
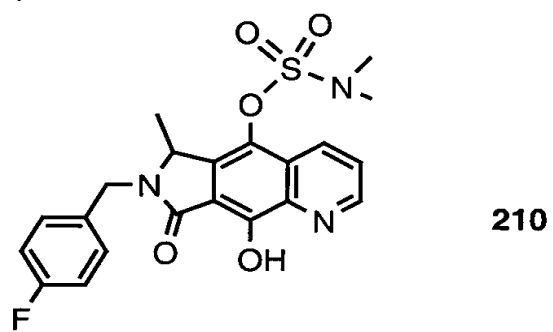
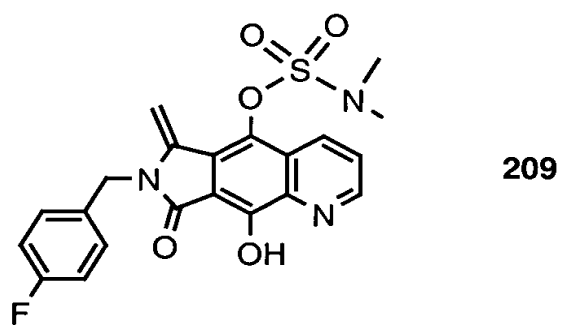


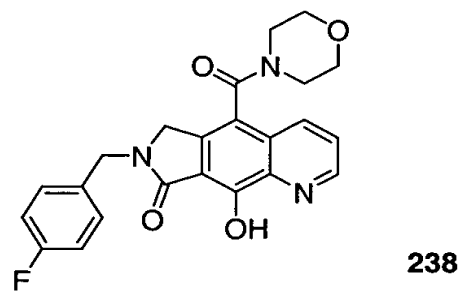
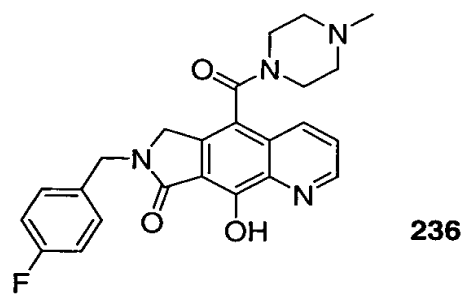
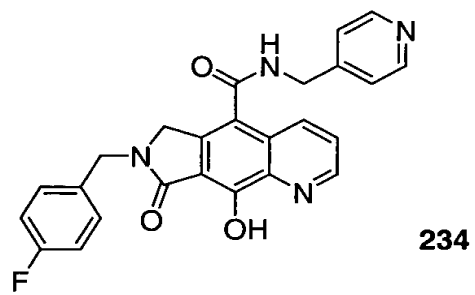
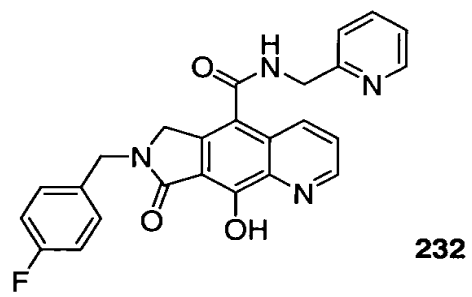
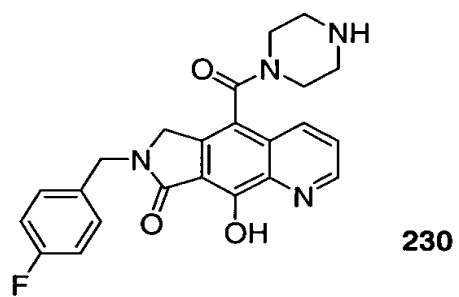


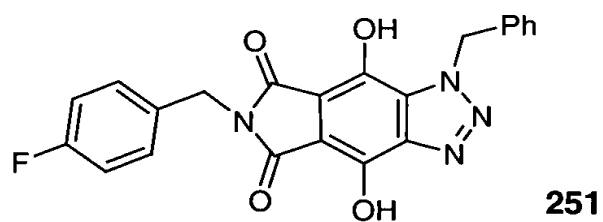
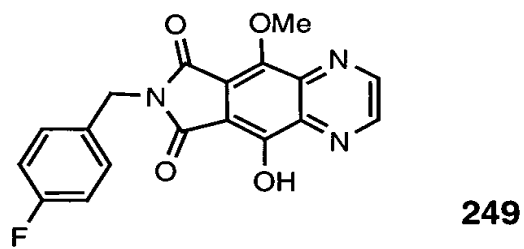
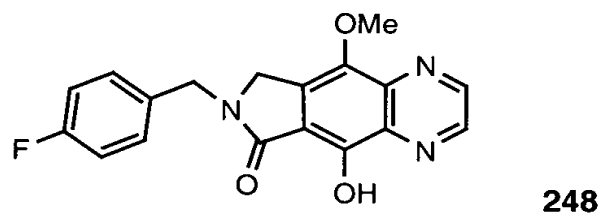
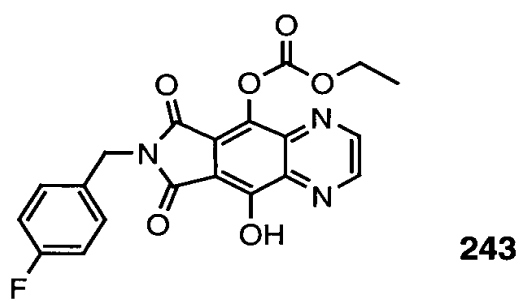
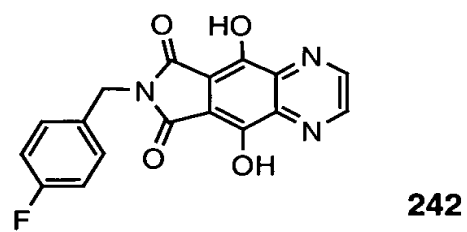
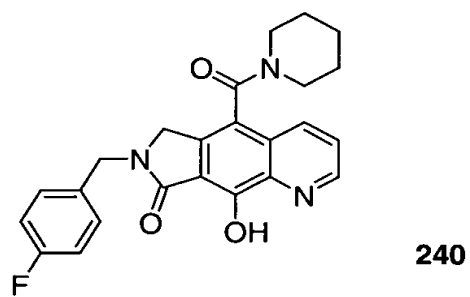


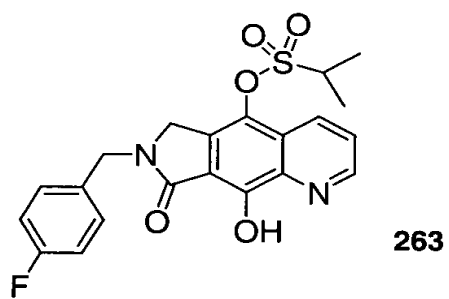
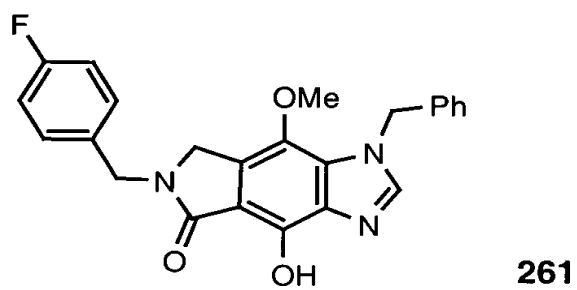
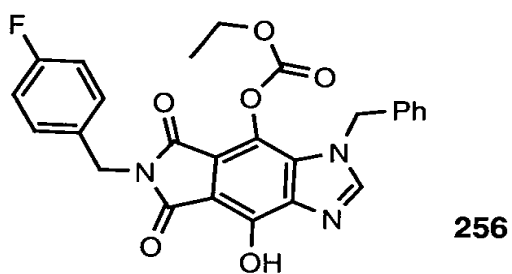
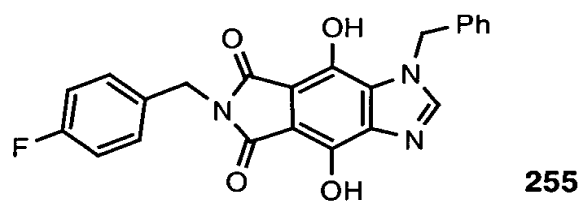
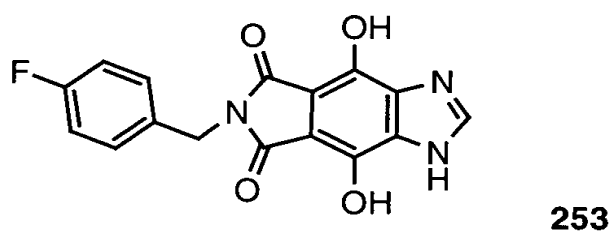


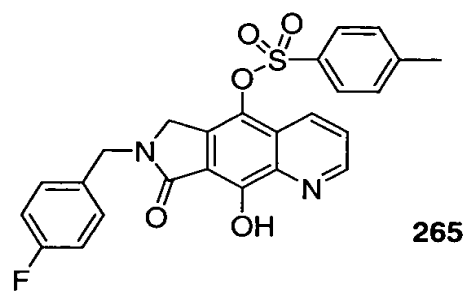




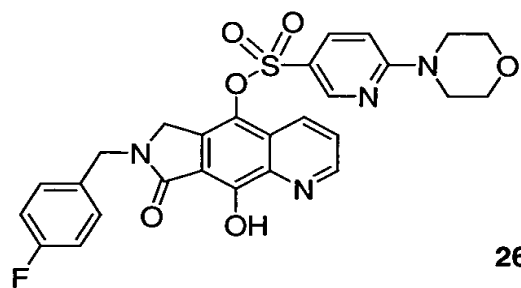




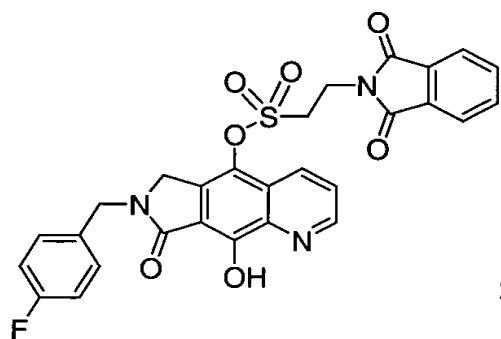




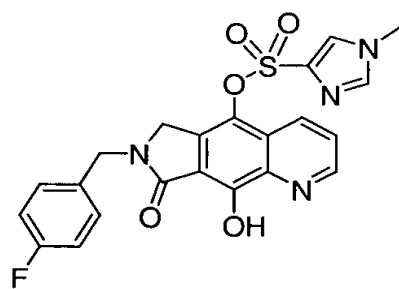
265



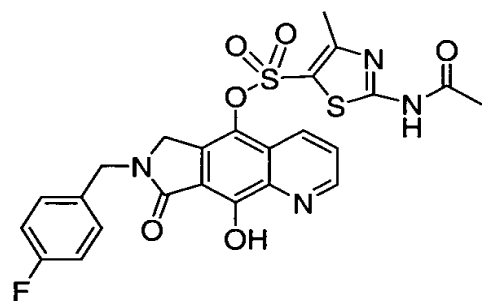
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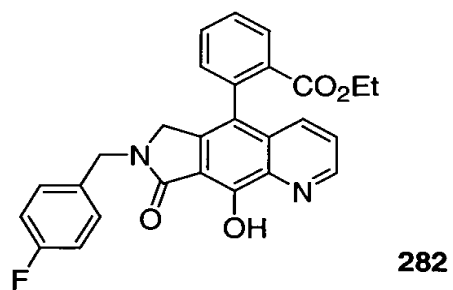
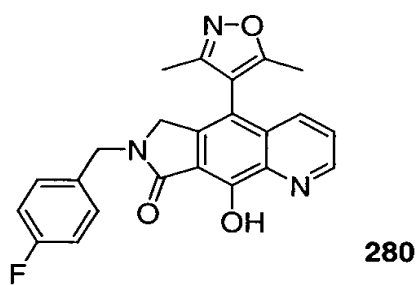
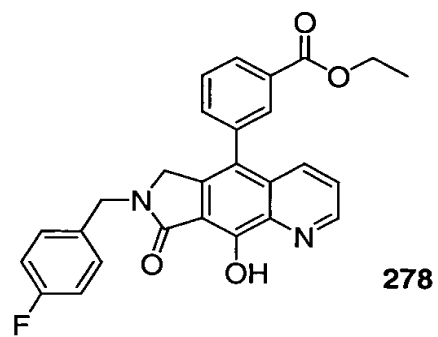
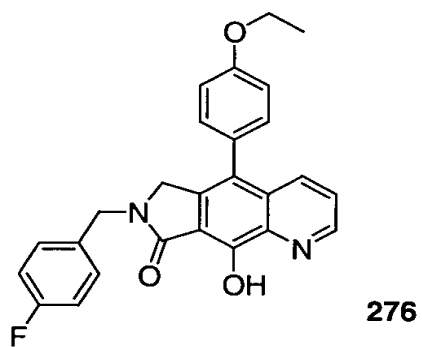
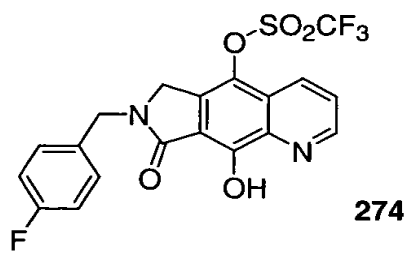
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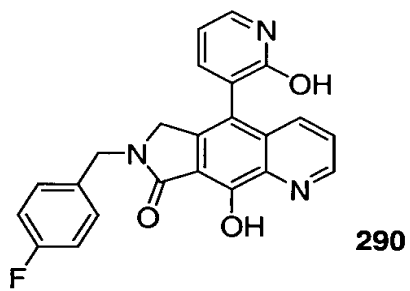
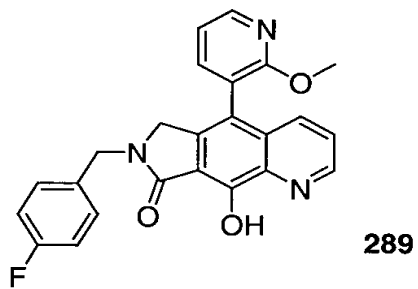
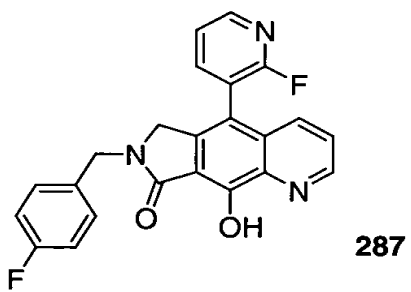
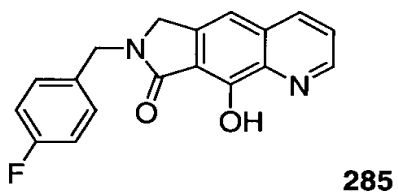
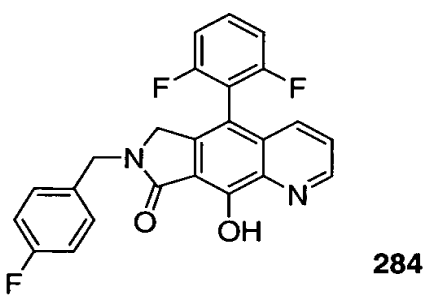


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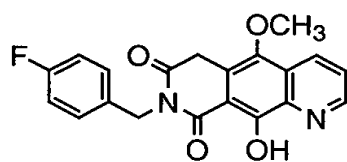


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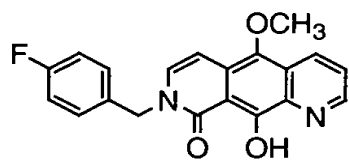




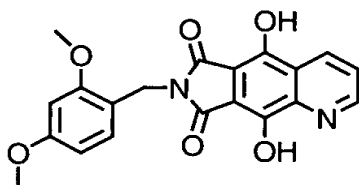




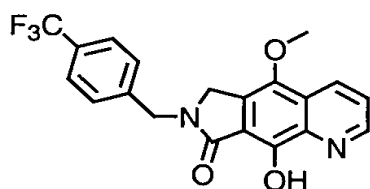
296



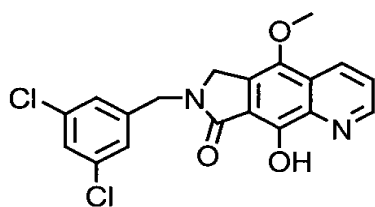
298



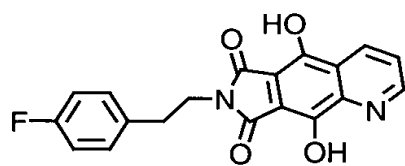
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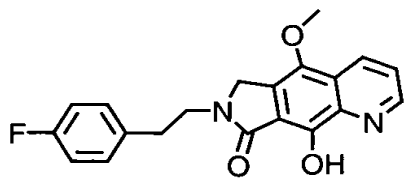
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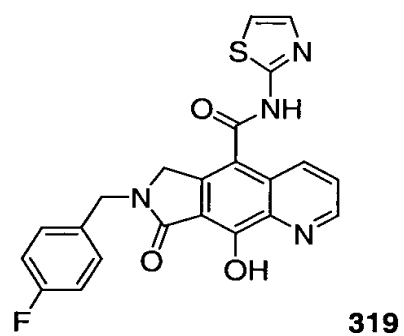
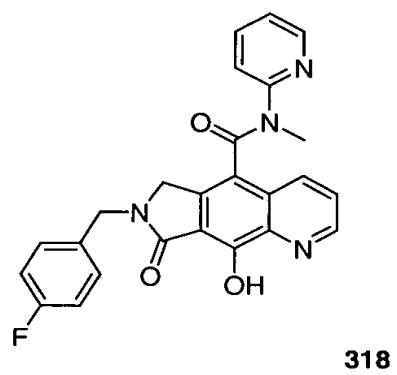
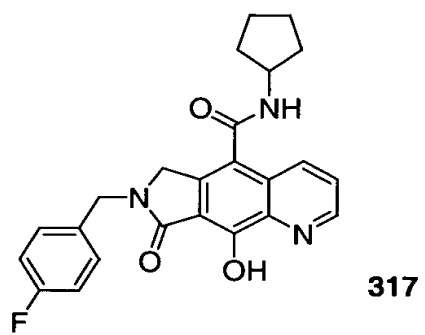
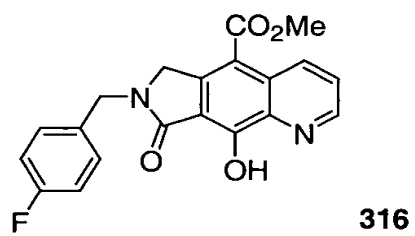
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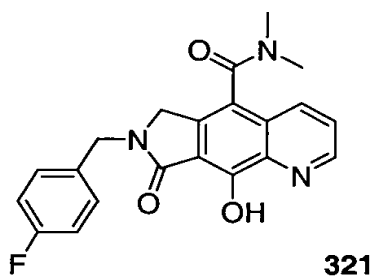
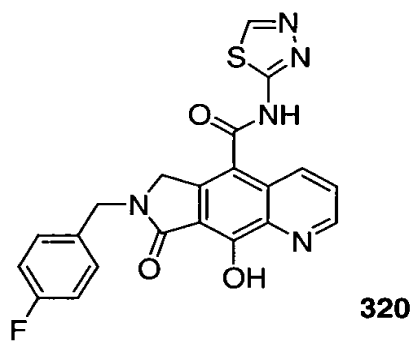


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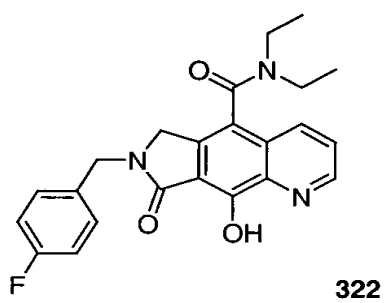


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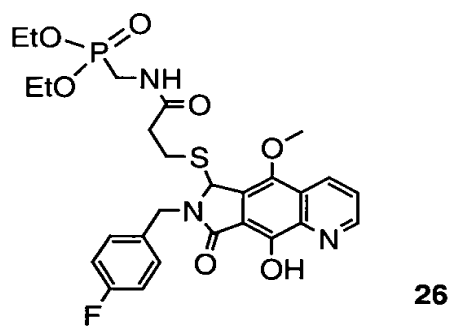


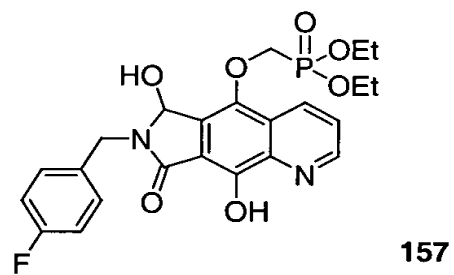
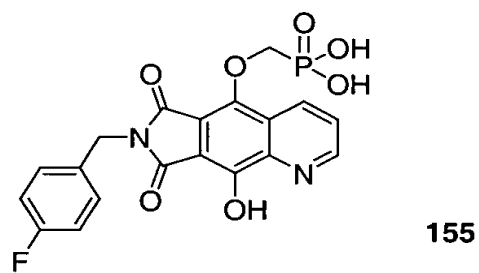
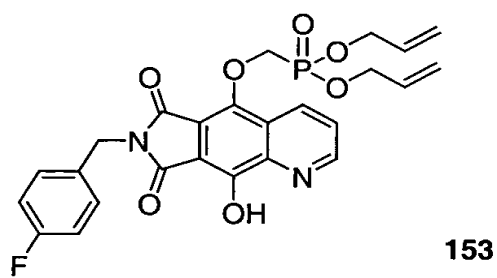
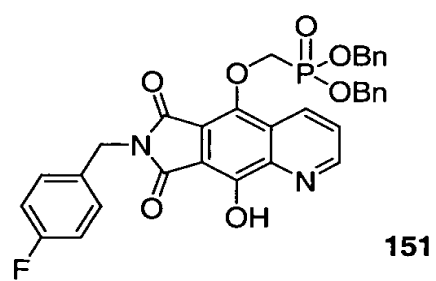
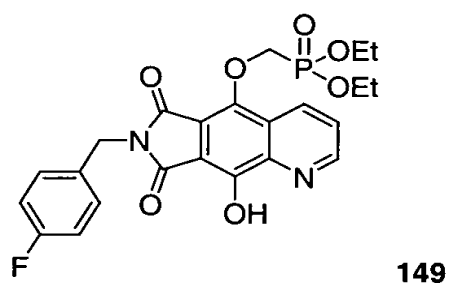


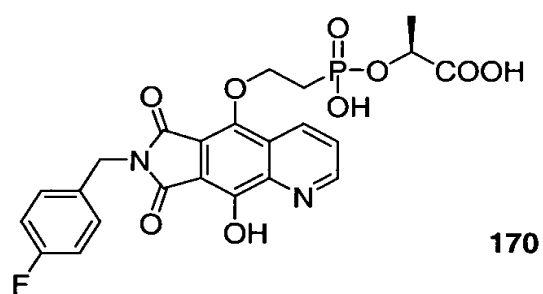
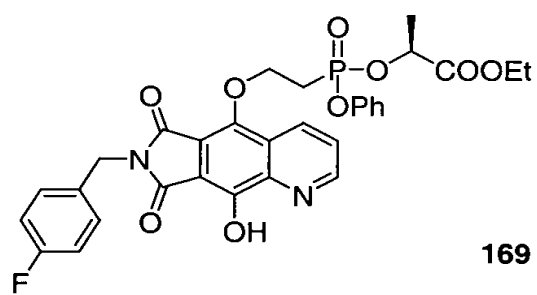
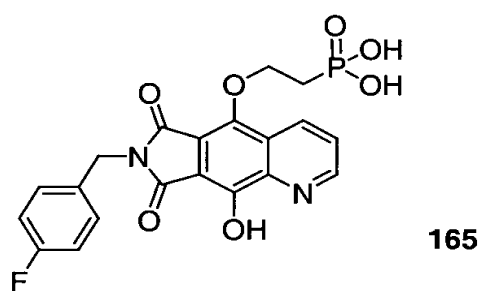
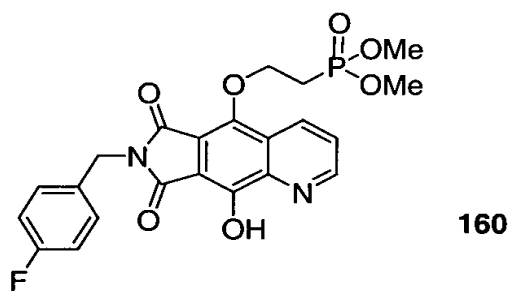
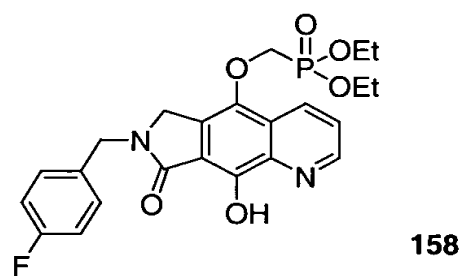
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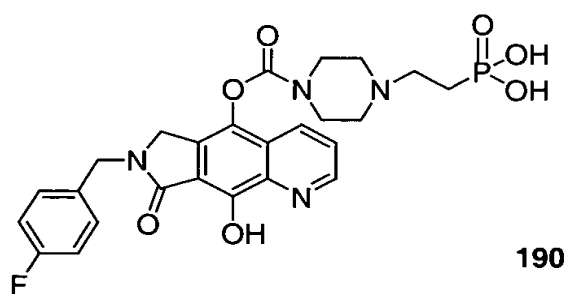
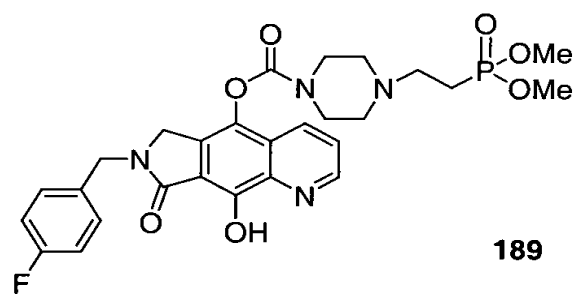
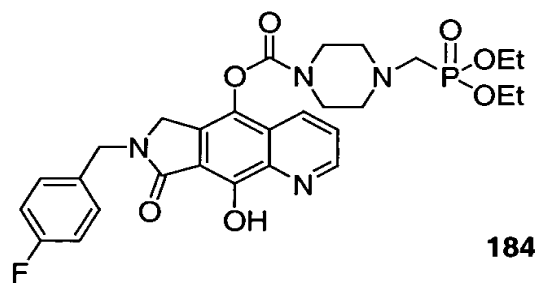
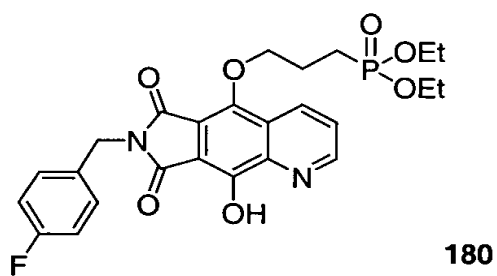
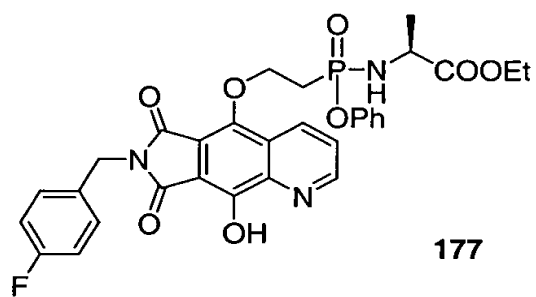


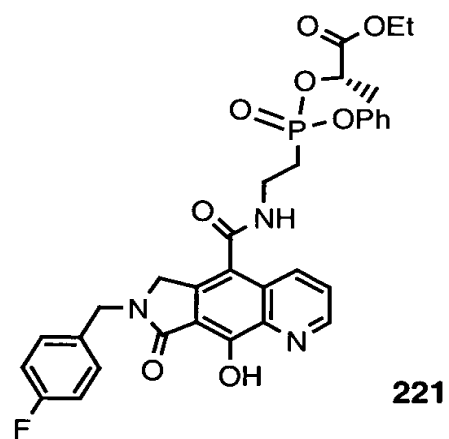
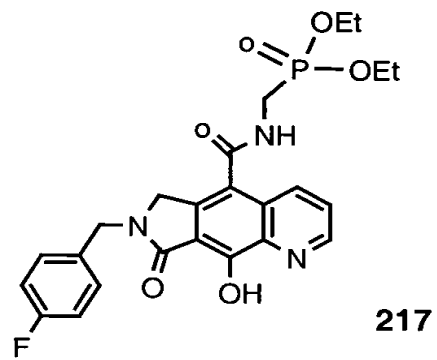
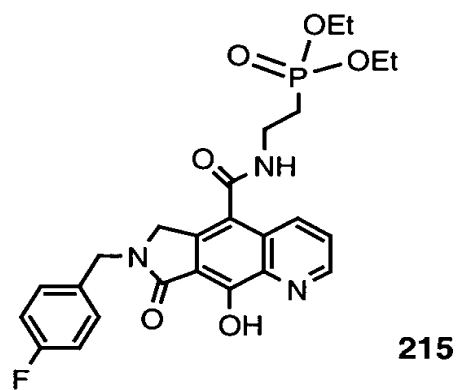
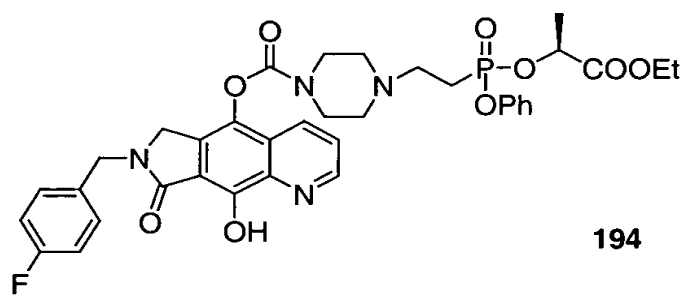
- 5      48.      A compound of claim 13 selected from the structures:

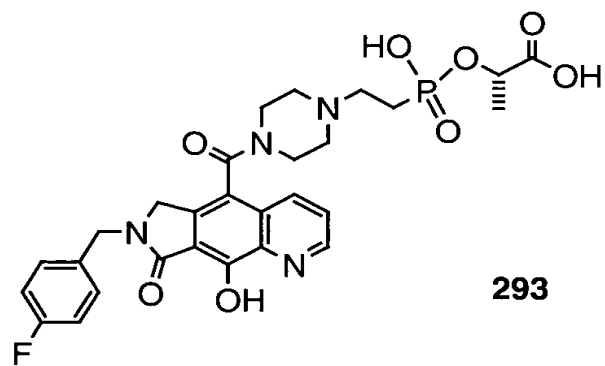
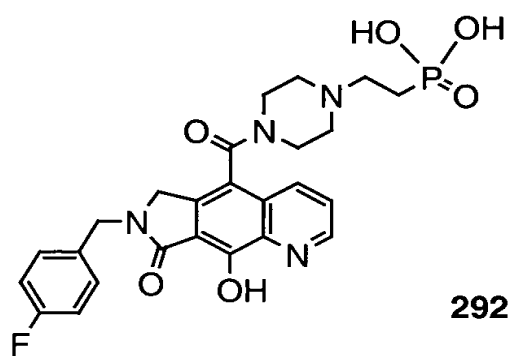
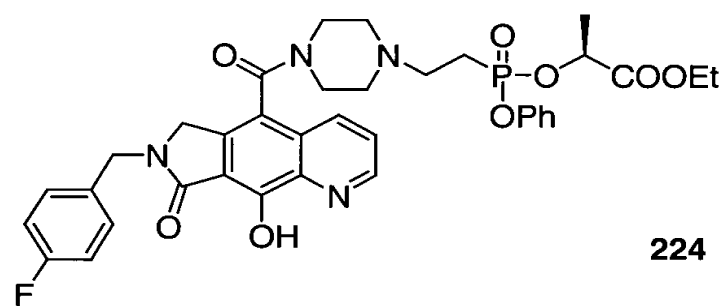
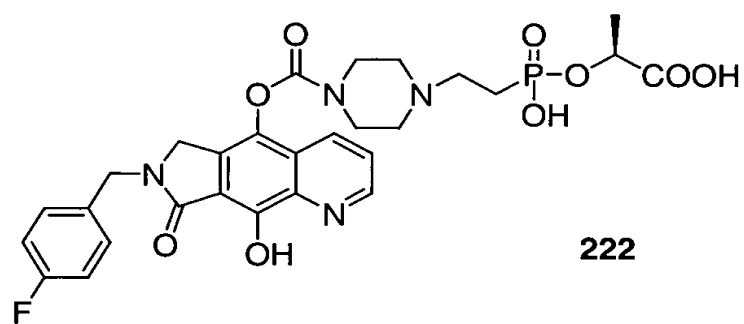




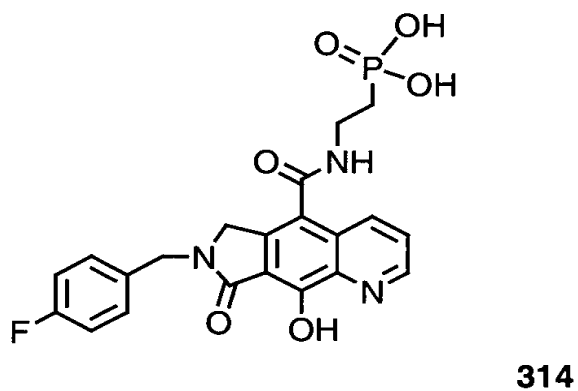
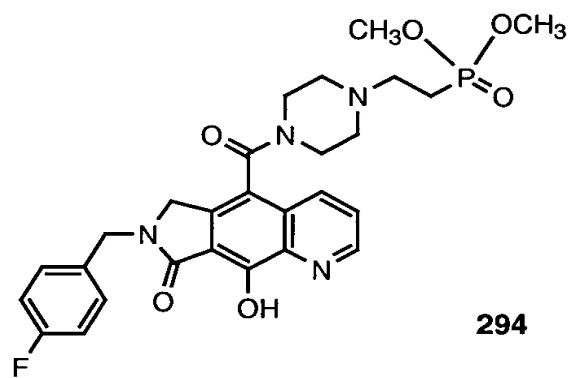




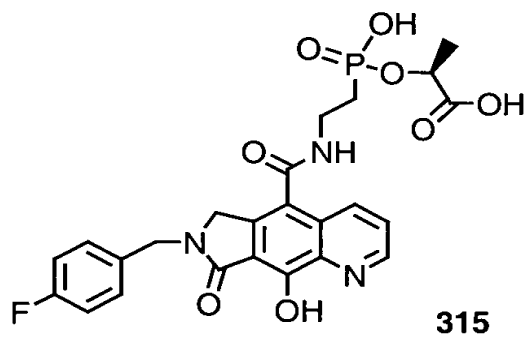




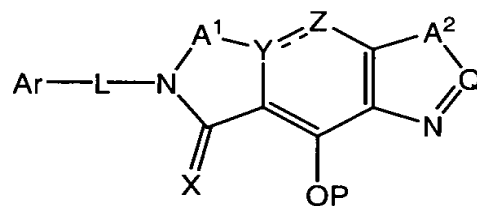




and



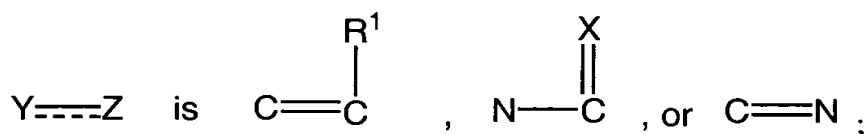
- 5      49.      A compound having the structure:



or a salt thereof;  
wherein:

$A^1$  and  $A^2$  are independently selected from O, S, NR,  $C(R^2)_2$ ,  $CR^2OR$ ,  $CR^2OC(=O)R$ ,  $C(=O)$ ,  $C(=S)$ ,  $CR^2SR$ ,  $C(=NR)$ ,  $C(R^2)_2-C(R^3)_2$ ,  $C(R^2)=C(R^3)$ ,  $NR-C(R^3)_2$ ,  $N=C(R^3)$ ,  $N=N$ ,  $SO_2-NR$ ,  $C(=O)C(R^3)_2$ ,  $C(=O)NR$ ,  $C(R^2)_2-C(R^3)_2-C(R^3)_2$ ,  $C(R^2)=C(R^3)-C(R^3)_2$ ,  $C(R^2)C(=O)NR$ ,  $C(R^2)C(=S)NR$ ,  $C(R^2)=N-C(R^3)_2$ ,  $C(R^2)=N-NR$ ,  
 5 and  $N=C(R^3)-NR$ ;

Q is N,  $^+NR$ , or  $CR^4$ ;



L is selected from a bond, O, S, S-S,  $S(=O)$ ,  $S(=O)_2$ ,  $S(=O)_2NR$ , NR, N-OR,  $C_1-C_{12}$  alkylene,  $C_1-C_{12}$  substituted alkylene,  $C_2-C_{12}$  alkenylene,  $C_2-C_{12}$  substituted  
 10 alkenylene,  $C_2-C_{12}$  alkynylene,  $C_2-C_{12}$  substituted alkynylene,  $C(=O)NH$ ,  $OC(=O)NH$ ,  $NHC(=O)NH$ ,  $C(=O)$ ,  $C(=O)NH(CH_2)_n$ , or  $(CH_2CH_2O)_n$ , where n may be 1, 2, 3, 4, 5, or 6;

X is selected from O, S, NH, NR, N-OR, N-NR<sub>2</sub>, N-CR<sub>2</sub>OR and N-CR<sub>2</sub>NR<sub>2</sub>;

Ar is selected from  $C_3-C_{12}$  carbocycle,  $C_3-C_{12}$  substituted carbocycle,  $C_6-C_{20}$  aryl,  $C_6-C_{20}$  substituted aryl,  $C_2-C_{20}$  heteroaryl, and  $C_2-C_{20}$  substituted heteroaryl;

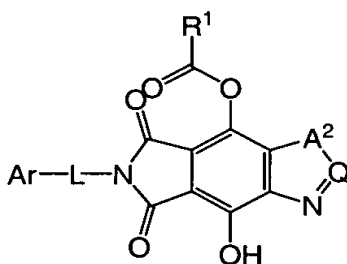
15  $R^1$ ,  $R^2$ ,  $R^3$  and  $R^4$  are each independently selected from H, F, Cl, Br, I, OH,  $-NH_2$ ,  $-NH_3^+$ ,  $-NHR$ ,  $-NR_2$ ,  $-NR_3^+$ ,  $C_1-C_8$  alkylhalide, carboxylate, sulfate, sulfamate, sulfonate, 5-7 membered ring sultam,  $C_1-C_8$  alkylsulfonate,  $C_1-C_8$  alkylamino, 4-dialkylaminopyridinium,  $C_1-C_8$  alkylhydroxyl,  $C_1-C_8$  alkylthiol,  $-SO_2R$ ,  $-SO_2Ar$ ,  $-SOAr$ ,  $-SAr$ ,  $-SO_2NR_2$ ,  $-SOR$ ,  $-CO_2R$ ,  $-C(=O)NR_2$ , 5-7 membered ring lactam, 5-7 membered ring  
 20 lactone,  $-CN$ ,  $-N_3$ ,  $-NO_2$ ,  $C_1-C_8$  alkoxy,  $C_1-C_8$  trifluoroalkyl,  $C_1-C_8$  alkyl,  $C_1-C_8$  substituted alkyl,  $C_3-C_{12}$  carbocycle,  $C_3-C_{12}$  substituted carbocycle,  $C_6-C_{20}$  aryl,  $C_6-C_{20}$  substituted aryl,  $C_2-C_{20}$  heteroaryl, and  $C_2-C_{20}$  substituted heteroaryl, polyethyleneoxy, phosphonate, phosphate, and a prodrug moiety;

when taken together on a single carbon, two  $R^2$  or two  $R^3$  may form a spiro ring;

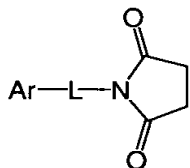
25 R is independently selected from H,  $C_1-C_8$  alkyl,  $C_1-C_8$  substituted alkyl,  $C_6-C_{20}$  aryl,  $C_6-C_{20}$  substituted aryl,  $C_2-C_{20}$  heteroaryl, and  $C_2-C_{20}$  substituted heteroaryl, polyethyleneoxy, phosphonate, phosphate, and a prodrug; and

P is a protecting group selected from benzyldryl ( $CHPh_2$ ), trialkylsilyl ( $R_3Si$ ), 2-trimethylsiloxyethyl, alkoxymethyl ( $CH_2OR$ ), and ester ( $C(=O)R$ ).

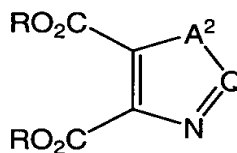
30 50. A process for preparation of a compound having the structure:



comprising reacting a succinimide compound having the structure:



5 with a heterocyclic compound having the structure:



and reaction with an acylation reagent comprising a formula selected from:



wherein:

10  $A^2$  is selected from O, S, NR,  $C(R^2)_2$ ,  $CR^2OR$ ,  $CR^2OC(=O)R$ ,  $C(=O)$ ,  $C(=S)$ ,  $CR^2SR$ ,  $C(=NR)$ ,  $C(R^2)_2-C(R^3)_2$ ,  $C(R^2)=C(R^3)$ ,  $NR-C(R^3)_2$ ,  $N=C(R^3)$ ,  $N=N$ ,  $SO_2-NR$ ,  $C(=O)C(R^3)_2$ ,  $C(=O)NR$ ,  $C(R^2)_2-C(R^3)_2-C(R^3)_2$ ,  $C(R^2)=C(R^3)-C(R^3)_2$ ,  $C(R^2)C(=O)NR$ ,  $C(R^2)C(=S)NR$ ,  $C(R^2)=N-C(R^3)_2$ ,  $C(R^2)=N-NR$ , and  $N=C(R^3)-NR$ ;

Q is N,  $^+NR$ , or  $CR^4$ ;

15 L is selected from a bond, O, S, NR, N-OR,  $C_1-C_{12}$  alkylidyl,  $C_1-C_{12}$  substituted alkylidyl,  $C(=O)NH$ ,  $C(=O)$ ,  $S(=O)$ ,  $S(=O)_2$ ,  $C(=O)NH(CH_2)_n$ , and  $(CH_2CH_2O)_n$ , where n ranges from 1 to 6;

Ar is selected from  $C_6-C_{20}$  aryl,  $C_6-C_{20}$  substituted aryl,  $C_2-C_{20}$  heteroaryl, and  $C_2-C_{20}$  substituted heteroaryl;

20  $R^1$  is selected from R, OR,  $NR_2$ ,  $NHR$ ,  $NHSO_2R$ , and  $NRSO_2R$ ;

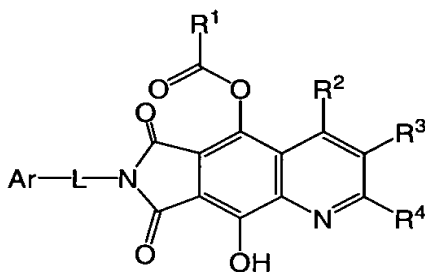
E is selected from Cl, imidazole, and hydroxybenzotriazole;

$R^2$ ,  $R^3$  and  $R^4$  are each independently selected from H, F, Cl, Br, I, OH,  $-NH_2$ ,  $-NH_3^+$ ,  $-NHR$ ,  $-NR_2$ ,  $-NR_3^+$ ,  $C_1-C_8$  alkylhalide, carboxylate, sulfate, sulfamate, sulfonate,

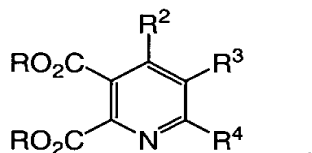
5-7 membered ring sultam, C<sub>1</sub>-C<sub>8</sub> alkylsulfonate, C<sub>1</sub>-C<sub>8</sub> alkylamino, 4-dialkylaminopyridinium, C<sub>1</sub>-C<sub>8</sub> alkylhydroxyl, C<sub>1</sub>-C<sub>8</sub> alkylthiol, -SO<sub>2</sub>R, -SO<sub>2</sub>Ar, -SOAr, -SAr, -SO<sub>2</sub>NR<sub>2</sub>, -SOR, -CO<sub>2</sub>R, -C(=O)NR<sub>2</sub>, 5-7 membered ring lactam, 5-7 membered ring lactone, -CN, -N<sub>3</sub>, -NO<sub>2</sub>, C<sub>1</sub>-C<sub>8</sub> alkoxy, C<sub>1</sub>-C<sub>8</sub> trifluoroalkyl, C<sub>1</sub>-C<sub>8</sub> alkyl, C<sub>1</sub>-C<sub>8</sub> substituted alkyl, C<sub>3</sub>-C<sub>12</sub> carbocycle, C<sub>3</sub>-C<sub>12</sub> substituted carbocycle, C<sub>6</sub>-C<sub>20</sub> aryl, C<sub>6</sub>-C<sub>20</sub> substituted aryl, C<sub>2</sub>-C<sub>20</sub> heteroaryl, and C<sub>2</sub>-C<sub>20</sub> substituted heteroaryl, polyethyleneoxy, phosphonate, phosphate, and a prodrug moiety; and

R is selected from C<sub>1</sub>-C<sub>6</sub> alkyl, C<sub>1</sub>-C<sub>6</sub> substituted alkyl, C<sub>6</sub>-C<sub>20</sub> aryl, C<sub>6</sub>-C<sub>20</sub> substituted aryl, C<sub>2</sub>-C<sub>20</sub> heteroaryl, C<sub>2</sub>-C<sub>20</sub> substituted heteroaryl, polyethyleneoxy, phosphonate, phosphate, and a prodrug moiety.

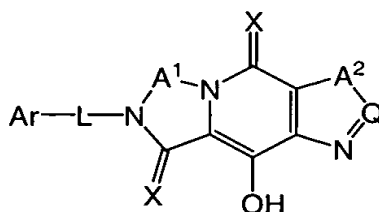
51. The process of claim 50 for preparation of a compound having the structure:



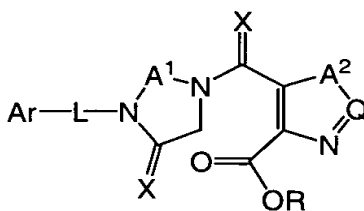
wherein the heterocyclic compound has the structure:



52. A process for preparation of a compound having the structure:



comprising reacting a compound having the structure:



with a basic reagent comprising hydroxide, an alkoxide or an amine;

wherein:

A<sup>1</sup> and A<sup>2</sup> are independently selected from O, S, NR, C(R<sup>2</sup>)<sub>2</sub>, CR<sup>2</sup>OR,

- 5 CR<sup>2</sup>OC(=O)R, C(=O), C(=S), CR<sup>2</sup>SR, C(=NR), C(R<sup>2</sup>)<sub>2</sub>-C(R<sup>3</sup>)<sub>2</sub>, C(R<sup>2</sup>)=C(R<sup>3</sup>), NR-C(R<sup>3</sup>)<sub>2</sub>, N=C(R<sup>3</sup>), N=N, SO<sub>2</sub>-NR, C(=O)C(R<sup>3</sup>)<sub>2</sub>, C(=O)NR, C(R<sup>2</sup>)<sub>2</sub>-C(R<sup>3</sup>)<sub>2</sub>-C(R<sup>3</sup>)<sub>2</sub>, C(R<sup>2</sup>)=C(R<sup>3</sup>)-C(R<sup>3</sup>)<sub>2</sub>, C(R<sup>2</sup>)C(=O)NR, C(R<sup>2</sup>)C(=S)NR, C(R<sup>2</sup>)=N-C(R<sup>3</sup>)<sub>2</sub>, C(R<sup>2</sup>)=N-NR, and N=C(R<sup>3</sup>)-NR;

Q is N, <sup>+</sup>NR, or CR<sup>4</sup>;

- 10 X is selected from O, S, NH, NR, N-OR, N-NR<sub>2</sub>, N-CR<sub>2</sub>OR and N-CR<sub>2</sub>NR<sub>2</sub>;

L is selected from a bond, O, S, NR, N-OR, C<sub>1</sub>-C<sub>12</sub> alkylidyl, C<sub>1</sub>-C<sub>12</sub> substituted alkylidyl, C(=O)NH, C(=O), S(=O), S(=O)<sub>2</sub>, C(=O)NH(CH<sub>2</sub>)<sub>n</sub>, and (CH<sub>2</sub>CH<sub>2</sub>O)<sub>n</sub>, where n ranges from 1 to 6;

Ar is selected from C<sub>6</sub>-C<sub>20</sub> aryl, C<sub>6</sub>-C<sub>20</sub> substituted aryl, C<sub>2</sub>-C<sub>20</sub> heteroaryl, and

- 15 C<sub>2</sub>-C<sub>20</sub> substituted heteroaryl;

R<sup>2</sup>, R<sup>3</sup> and R<sup>4</sup> are each independently selected from H, F, Cl, Br, I, OH, -NH<sub>2</sub>,

-NH<sub>3</sub><sup>+</sup>, -NHR, -NR<sub>2</sub>, -NR<sub>3</sub><sup>+</sup>, C<sub>1</sub>-C<sub>8</sub> alkylhalide, carboxylate, sulfate, sulfamate, sulfonate, 5-7 membered ring sultam, C<sub>1</sub>-C<sub>8</sub> alkylsulfonate, C<sub>1</sub>-C<sub>8</sub> alkylamino, 4-

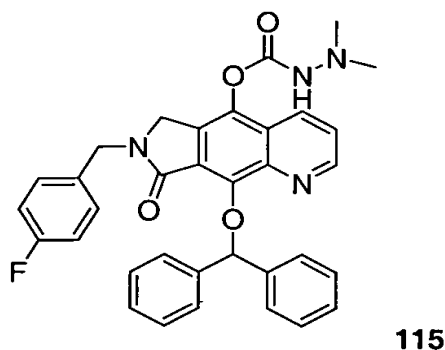
dialkylaminopyridinium, C<sub>1</sub>-C<sub>8</sub> alkylhydroxyl, C<sub>1</sub>-C<sub>8</sub> alkylthiol, -SO<sub>2</sub>R, -SO<sub>2</sub>Ar, -SOAr,

- 20 -SAr, -SO<sub>2</sub>NR<sub>2</sub>, -SOR, -CO<sub>2</sub>R, -C(=O)NR<sub>2</sub>, 5-7 membered ring lactam, 5-7 membered ring lactone, -CN, -N<sub>3</sub>, -NO<sub>2</sub>, C<sub>1</sub>-C<sub>8</sub> alkoxy, C<sub>1</sub>-C<sub>8</sub> trifluoroalkyl, C<sub>1</sub>-C<sub>8</sub> alkyl, C<sub>1</sub>-C<sub>8</sub> substituted alkyl, C<sub>3</sub>-C<sub>12</sub> carbocycle, C<sub>3</sub>-C<sub>12</sub> substituted carbocycle, C<sub>6</sub>-C<sub>20</sub> aryl, C<sub>6</sub>-C<sub>20</sub> substituted aryl, C<sub>2</sub>-C<sub>20</sub> heteroaryl, and C<sub>2</sub>-C<sub>20</sub> substituted heteroaryl, polyethyleneoxy, phosphonate, phosphate, and a prodrug moiety; and

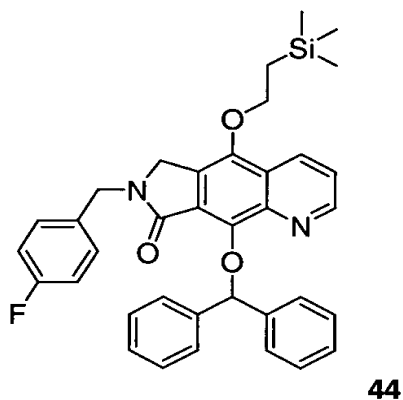
25 R is selected from C<sub>1</sub>-C<sub>6</sub> alkyl, C<sub>1</sub>-C<sub>6</sub> substituted alkyl, C<sub>6</sub>-C<sub>20</sub> aryl, C<sub>6</sub>-C<sub>20</sub>

substituted aryl, C<sub>2</sub>-C<sub>20</sub> heteroaryl, C<sub>2</sub>-C<sub>20</sub> substituted heteroaryl, polyethyleneoxy, phosphonate, phosphate, and a prodrug moiety.

53. A process for preparation of a compound having structure 115:



comprising reacting a compound having the structure 44:



with tetrabutylammonium fluoride to form a desilylated intermediate; and  
 5 reacting the desilylated intermediate with triphosgene (bis(trichloromethyl) carbonate), followed by dimethylhydrazine to form structure 115.

54. A compound of claim 1 comprising a phosphonate prodrug and capable of accumulating in human PBMC.

10 55. The compound of claim 54 wherein the bioavailability of the compound or an intracellular metabolite of the compound in human PBMC is improved when compared to the analog of the compound not having the phosphonate or phosphonate prodrug.

15 56. The compound of claim 54 wherein the intracellular half-life of the compound or an intracellular metabolite of the compound in human PBMC is improved when compared to the analog of the compound not having the phosphonate or phosphonate prodrug.

57. The compound of claim 56 wherein the half-life is improved by at least about 50%.

58. The compound of claim 56 wherein the half-life is improved by at least about 100%.

59. The compound of claim 54 wherein the intracellular half-life of a metabolite of the compound in human PBMC is improved when compared to an analog of the compound not having the phosphonate or phosphonate prodrug.

60. The compound of claim 59 wherein the half-life is improved by at least about 50%.

61. The compound of claim 59 wherein the half-life is improved by at least about 100%.

62. The compound of claim 59 wherein the half-life is improved by greater than 100%.

63. A pharmaceutical composition comprising a therapeutically effective amount of a compound of claim 1 and a pharmaceutically acceptable carrier.

64. The pharmaceutical composition of claim 62 further comprising a therapeutically effective amount of an AIDS treatment agent selected from an HIV inhibitor agent, an anti-infective agent, and an immunomodulator.

65. The pharmaceutical composition of claim 64 wherein the HIV inhibitor agent is an HIV-protease inhibitor.

66. The composition of claim 64 wherein the HIV inhibitor agent is a nucleoside reverse transcriptase inhibitor.

67. The composition of claim 64 wherein the HIV inhibitor agent is a non-nucleoside reverse transcriptase inhibitor.

68. A process for making a pharmaceutical composition comprising combining a compound of claim 1 and a pharmaceutically acceptable carrier.

69. A method of inhibiting HIV integrase, comprising the administration to a mammal in need of such treatment of a therapeutically effective amount of a compound of claim 1.

70. A method of treating infection by HIV, or of treating AIDS or ARC, comprising administration to a mammal in need of such treatment of a therapeutically effective amount of a compound of claim 1.

71. Method of treating a disorder affecting white blood cells, comprising:  
administering a compound of claim 1 comprising phosphonate prodrug to a patient in need of white-blood-cell targeting.

72. Method of targeting a compound to white blood cells, comprising:  
selecting a compound of claim 1 having a desired pharmaceutical activity and having a first structure;  
modifying said first structure by replacing one or more atom of said first structure with an organic substituent comprising a phosphonate group or incipient phosphonate group to provide a compound having a second structure.

73. A method of manufacturing an HIV inhibitor compound having both selectivity for white blood cells and a desired pharmaceutical activity, comprising:  
chemically synthesizing a first molecule of claim 1 having a first structure containing a phosphonate or precursor phosphonate group, wherein said first structure differs from a second structure of a compound known to have said desired pharmaceutical activity by having at least one hydrogen atom of said second structure replaced by an organic substituent comprising a phosphonate group or incipient phosphonate group.

74. The method of claim 73, wherein said first molecule is synthesized by a series of chemical reactions in which a hydrogen of said second structure is replaced by said organic substituent.

75. The method of claim 73, wherein said first molecule is synthesized by a series of chemical reactions that never includes a molecule of said second structure.

76. Method of accumulating an HIV integrase inhibitor compound inside a white blood cell, comprising:  
administering to a sample a composition comprising a compound of claim 1.

77. The method of claim 75 wherein said sample is a patient.

78. The method of claim 73, wherein said compound has a chemical structure A-B, wherein (a) a compound having structure A-H has HIV integrase inhibitor activity and (b) substructure B comprises a phosphonate group or a precursor phosphonate group.



79. Method of increasing half-life of an HIV integrase inhibitor compound, comprising:

replacing at least one hydrogen atom or organic radical of a compound of claim 1 by an organic substituent comprising a phosphonate group or incipient phosphonate.